CHEMICAL HERITAGE FOUNDATION

YUSUF A. HANNUN

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Neil D. Hathaway

at

Duke University Medical Center & The Home of Yusuf Hannun
Durham and Chapel Hill, North Carolina

on

29, 30 March and 1, 2 April 1993

From the Original Collection of the University of California, Los Angeles

Yusuf A. Hannun

ACKNOWLEDGEMENT

This oral history is part of a series supported by a grant from the Pew Charitable Trusts based on the Pew Scholars Program in the Biomedical Sciences. This collection is an important resource for the history of biomedicine, recording the life and careers of young, distinguished biomedical scientists and of Pew Biomedical Scholar Advisory Committee members.

This oral history was completed under the auspices of the Oral History Project, University of California, Los Angeles (Copyright © 1993, The Regents of the University of California) and is made possible through the generosity of

From the original collection at the Center for Oral History Research, UCLA Library, UCLA.

The following oral history, originally processed at the UCLA Center for Oral History Research, has been reformatted by the Chemical Heritage Foundation. The process involved reformatting the front matter, adding a new abstract, replacing the table of contents, and replacing the index. The paragraph spacing and font of the body of the transcript were altered to conform to the standards of the Oral History Program at the Chemical Heritage Foundation. The text of the oral history remains unaltered; any inadvertent spelling or factual errors in the original manuscript have not been modified. The reformatted version and digital copies of the interview recordings are housed at the Othmer Library, Chemical Heritage Foundation. The original version and research materials remain at the Darling Library, University of California, Los Angeles and at the Bancroft Library, University of California, Berkeley.

REFORMATTING:

Kim Phan, Program Intern, Oral History, Chemical Heritage Foundation. B.A. expected 2011, Anthropology, Cornell University.

David J. Caruso, Program Manager, Oral History, Chemical Heritage Foundation. B.A., History of Science, Medicine, and Technology, Johns Hopkins University; PhD., Science and Technology Studies, Cornell University.

UNIVERSITY OF CALIFORNIA, LOS ANGELES

Oral History Interview Agreement No. R930407

This Interview Agreement is made and entered into this 9th day of April, 1993, by and between THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, a California corporation, on behalf of the Oral History Program at the UCLA campus, hereinafter called "University," and YUSUF A. HANNUN having an address at Duke University Medical Center, Department of Hematology/Oncology, Box 3355, DUMC, Durham, North Carolina, 27710, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about March 29, 1993, and tentatively entitled "Interview with Yusuf A. Hannun". This Agreement relates to any and all materials originating from the interviews, namely the tape recordings of the interviews and a written manuscript prepared from the tapes, hereinafter collectively called "the Work."

In consideration of the mutual covenants, conditions, and terms set forth below, the parties hereto hereby agree as follows:

1. Interviewee irrevocably assigns to University all his copyright, title and interest in and to the Work. This assignment applies to University, its successors, and assigns, for and during the existence of the copyright and all renewals and extensions thereof.

2. By virtue of this assignment, University will have the right to use the Work for any research, educational, or other purpose that University may deem appropriate.

3. Interviewee acknowledges that he will receive no remuneration or compensation for his participation in the interviews or for the rights assigned hereunder.

4. Interviewee will receive from University, free of charge, one bound copy of the typewritten manuscript of the interviews.

5. To insure against substantive error or misquotation, Interviewee will have the right to review the manuscript before it is put into final form. University therefore will send Interviewee a copy of the edited transcript for review and comment. Interviewee will return transcript and comments to University within 30 days of receipt of the transcript. In the event that Interviewee does not respond within 30 days, University will assume that Interviewee has given full approval of the transcript.

6. All notices and other official correspondence concerning this Agreement will be sent to the following:

If to University : Office of Intellectual Property Administration
University of California, Los Angeles
405 Hilgard Avenue
Los Angeles, California 90024-1406

Attention: Ms. Carli V. Rogers
Copyright Officer

If to Interviewee: Yusuf A. Hannun
Duke University Medical Center
Department of Hematology/Oncology
Box 3355
Durham, NC 27710

University and Interviewee have executed this Agreement on the date first written above.

INTERVIEWEE

Signed release form is on file at the Science History Institute
(Signature)

Yusuf A. Hannun
(Typed Name)

Duke University Medical Center

Box 3355, DUMC
(Address)

Durham, NC 27710

Date April 1, 1993

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

Signed release form is on file at the Science History Institute
(Signature)

Carli V. Rogers
(Typed Name)

Copyright Officer
(Title)

Date April 9, 1993

PERMISSION TO POST COMPLETED ORAL HISTORY TRANSCRIPT AND/OR INTERVIEW RECORDINGS ON THE INTERNET

The original release agreement that you signed with the Science History Institute, which governs researchers' access to your oral history, either made no mention of posting your entire transcript and/or interview recordings on our website or stipulated that we would seek your permission before posting the full interview. It is our goal to broaden individuals' access to the Science History Institute's oral histories generally, and your oral history specifically, so we are contacting you to request permission to post your entire completed transcript and interview recordings on our website, located at http://www.sciencehistory.org and on the Science History Institute's Digital Collections website, located at https://digital.sciencehistory.org/. To be clear, if you requested that certain sections of your interview be restricted or sealed, they will not be included in the material posted to the Internet and will remain restricted/sealed as outlined in the original release agreement.

Should you choose to grant us permission to post your entire completed transcript and interview recordings, the Science History Institute will not be able to limit anyone's access to or use of your oral history in any way outside the bounds of U.S. Copyright Law under title 17 of the United States Code.

If you have any questions about this form, or if you would like to review your original release agreement, please contact the Director of the Center for Oral History at oralhistory@sciencehistory.org; (215) 925-2222; or Director, Center for Oral History, Science History Institute, 315 Chestnut Street, Philadelphia, PA 19106.

__YAH_____ Initials

I, Yusuf Hannun, GRANT exclusive permission to the Science History Institute to post my completed oral history transcript and interview recordings conducted on 29, 30 March and 1, 2 April 1993 with Neil D. Hathaway at Duke University Medical Center & The Home of Yusuf Hannun on the Science History Institute's website.

_____ Initials

I, Yusuf Hannun, DO NOT GRANT permission to the Science History Institute to post my completed oral history transcript and interview recordings conducted on 29, 30 March and 1, 2 April 1993 with Neil D. Hathaway at Duke University Medical Center & The Home of Yusuf Hannun on the Internet during my lifetime.

Signature: Signed release form is on file at the Science History Institute
Interviewee's Name

10.7.2021_____
Date

Errata

The following errors have been identified in Yusaf A. Hannun's transcript:

- Page 7: "This isn't such a planned or traditional way of doing things in Palestinian culture."
- Page 12: "I assume that this also was true maybe in school . . ."
- Page 14: "And I don't mean to be glib about it . . ."
- Page 26: "I just didn't have that aspiration."
- Page 32: "I would say a few were, but most were not."
- Page 33: "The way I look at the Lebanese conflict, again, just to sort of put things in context . . ."
- Page 42: "When he started out, that was in the late twenties."
- Page 47: "But I resented the fact that I had to be in this kind of rat race."
- Page 50: "Obviously, I couldn't see myself idle in London."
- Page 56: "They're more of a nuisance than a help, right?"
- Page 58: "I think that maybe, in talking a lot about the educational part of getting there . . ."
- Page 71: "I told you the other day, too . . ."
- Page 74: "So my expectations were not high.
- Page 78: "He actually thought that the . . ."
- Page 102: "No, I think of it more in terms of I'm contributing to how people understand things."
- Page 109: "It's a hot area, absolutely."
- Page 112: ". . . went through just the regular NIH channels and whatnot . . ."
- Page 113: "Mallinckrodt [scholar]."
- Page 115: ". . . is the R01 given out by NIH, the individual research proposal."
- Page 117: ". . . again, like the R01 is the backbone of biomedical research . . ."
- Page 117: ". . . to really put major force on the R01 system."
- Page 118: "I could be a biochemist studying E. coli . . ."
- Page 122: ". . . instead of saying—"
- Page 124: "I mean, how HHMI perceives its role."
- Page 124: "So the Nobel Prize I don't think should be a goal . . ."
- Page 130: "I don't know how major."
- Page 136: "I mean, the British do it with probably thirty hours a week."
- Page 137: "It has its merits; it has its downsides."
- Page 140: "I don't have anything absolutely vital . . ."
- Page 147: "I guess I see that as not the common way that labs are built."
- Page 149: ". . . and everyone listens. [laughter]"
- Page 157: "I mean, that's not bad for those who like to do that."
- Page 158: "No problem."

Chemical Heritage Foundation
Oral History Program
315 Chestnut Street
Philadelphia, Pennsylvania 19106

YUSUF A. HANNUN

1955 Born in Dahran, Saudi Arabia, on 18 September

Education

1977 B.Sc., Biology/Chemistry, American University of Beirut
1981 M.D., American University of Beirut

Professional Experience

Duke University Medical Center
1983-1986 Hematology/Oncology Fellow
1987-1992 Assistant Professor, Department of Medicine
1989-1992 Assistant Professor, Department of Cell Biology
1992-present Associate Professor, Department of Medicine

Honors

1980 Alpha Omega Alpha
1985-1990 Physician Scientist Award, National Institutes of Health
1988-1992 Pew Scholars Program in the Biomedical Sciences Grant
1990-1995 Established Investigator Award, American Heart Association
1990-1993 Mallinckrodt Scholar
1991 American Society for Clinical Investigation
1992 R. Wayne Rundles Award for Excellence in Cancer Research

Selected Publications

Hannun, Y.A., et al., 1984. Emergency valve replacement during acute carditis--case reports. *Middle East Journal of Anesthesiology,* 7:363-71.

Hannun, Y.A. and R. Frayha, 1985. Behget's disease with pseudochylothorax. *Journal of Rheumatism,* 12:817-18.

Hannun, Y.A., et al., 1990. Long-term survival in patients treated for testicular cancer. *Journal of Surgical Oncology,* 43:117-80.

Hannun, Y.A., et al., 1985. Activation of protein kinase C by triton X-100 mixed micelles containing diacylglycerol and phosphatidylserine. *Journal of Biological Chemistry,* 260:10039-43.

Hannun, Y.A., et al., 1986. Protein kinase C activation in mixed micelles: Mechanistic

implications of phospholipid, diacylglycerol, and calcium interdependencies. *Journal of Biological Chemistry,* 261:7184-90.
Hannun, Y.A. and R.M. Bell, 1986. Phorbol ester binding and activation of protein kinase C in triton X-100 containing phosphatidylserine. *Journal of Biological Chemistry,* 261:9341-47.
Hannun, Y.A., et al., 1986. Sphingosine inhibition of protein kinase C activity and of phorbol dibutryate binding *in vitro* and in human platelets. *Journal of Biological Chemistry,* 261:12604-9.
Hannun, Y.A. and R.M. Bell, 1987. Mixed micellar assay for phorbol ester binding. In *Methods in Enzymology,* ed. M. Conn. Academic Press, 141:287-94.
Hannun, Y.A. and R.M. Bell, 1987. Lysosphingolipid inhibition of protein kinase C: Implications in the pathogenesis of sphingolipidoses. *Science,* 235:670-74.
Hannun, Y.A. and R.M. Bell, 1987. Mechanism of activation of protein kinase C: Role of diacylglycerol and calcium second messengers. In Cell *Calcium and the Control of Membrane Transport,* eds. L. Mandel and E. Eaton. New York: Rockefeller University Press, 42:230-40.
Hannun, Y.A., et al., 1987. Sphingosine inhibition of agonist dependent secretion and activation of human platelets implies that protein kinase C is a necessary and common event in the signal transduction pathway. *Journal of Biological Chemistry,* 262:13620-26.
Hannun, Y.A. and R.M. Bell1988. Aminiacridines: Potent inhibitors of protein kinase C. *Journal of Biological Chemistry,* 263:5124-31.
Bell, R.M., C.R. Loomis, and Y.A. Hannun, 1988. Protein kinase C regulation by sphingosine/lysosphingolipids. *Cold Spring Harbor Symposia on Quantitative Biology,* 53:103-10.
Hannun, Y.A. and R.M. Bell, 1989. Functions of sphingolipids and sphingolipid breakdown products in cellular regulation. *Science,* 243:500-507.
Hannun, Y.A., R. Fogelsong, and R.M. Bell, 1989. The adriamycin-iron III complex is a potent inhibitor of protein kinase C. *Journal of Biological Chemistry,* 264:9960-66.
Okazaki, T., R.M. Bell, and Y.A. Hannun, 1989. Sphingomyelin turnover induced by vitamin D_3 in HL-60 cells: Role in cell differentiation. *Journal of Biological Chemistry,* 264:19076-80.
Sane, D., A. Bielawska, C. Greenberg, and Y.A. Hannun, 1989. Cyclic GMP analogs inhibit gamma thrombin-induced arachidonic acid release in human platelets. *Biochemical and Biophysical Research Communications,* 165:708-14.
Hannun, Y.A., 1989. Sphingomyelin synthase and PKC activation. *Science,* 264:1049.
Hannun, Y.A. and R.M. Bell, 1989. Regulation of protein kinase C by sphingosine and lysosphingolipids. *Clinica Chemica Acta,* 185:333-46.
Hannun, Y.A. and R.M. Bell, 1990. Rat brain protein kinase C: Kinetic analysis of substrate dependence, allosteric regulation, and autophosphorylation. *Journal of Biological Chemistry,* 265:2962-72.
Obeid, L.M., T. Okazaki, L. Karolak, and Y.A. Hannun, 1990. Transcriptional regulation of protein kinase C by 1,25-dihydroxyvitamin D_3 in HL-60 cells. *Journal of Biological Chemistry,* 265:2370-4.
Okazaki, T., A. Bielawska, R.M. Bell, and Y.A. Hannun, 1990. Role of ceramide as a second messenger in HL-60 cell differentiation induced by la,25-dihydroxyvitamin D_3. *Journal of Biological Chemistry,* 265:15823-31.
El Touny, S., W. Khan, and Y.A. Hannun, 1990. Regulation of protein kinase C by oleic acid: Kinetic analysis of allosteric regulation and effects on autophosphorylation, phorbol ester

binding, and susceptibility to inhibition. *Journal of Biological Chemistry,* 265:16437-43.
Khan, *W.*, R. Dobrowsky, S. El Touny, and Y.A. Hannun, 1990. Protein kinase C and platelet inhibition by Derythro-sphingosine: Comparison with N,N-dimethylsphingosine and commercial preparation. *Biochemical and Biophysical Research Communications,* 172:683 91.
Hannun, Y.A., 1991. Sphingolipid metabolism and biology. In *Encyclopedia of Human Biology. Academic* Press, 7:17989.
Hannun, Y.A., 1991. Regulation of protein kinase C. In *Eicosanoids and Other Bioactive Lipids in Cancer and Radiation Injury,* eds. K.V. Honn, L.J. Marnett, S. Nigam, and T. Walden, Jr. Boston: Kluwer Academic Publishers, 275-83.
Hannun, Y.A., A. Merrill, and R.M. Bell, 1991. Use of sphingosine as an inhibitor of protein kinase C. In *Method in Enzymology,* eds. T. Hunter and B. Sefton. Academic Press, 201:316 28.
Kim, M.Y., C. Linardic, L. Obeid, and Y.A. Hannun, 1991. Identification of sphingomyelin turnover as an effector mechanism for the action of TNF a and y interferon; specific role in cell differentiation. *Journal of Biological Chemistry,* 266:484-89.
Bell, R.M., T. Okazaki, and Y.A. Hannun, 1991. Lipid second messengers: Protein kinase C dependent and independent pathways. In Proceedings of the 12th *International RES Congress and* 27th *Annual Meeting of* the *Society for Leukocyte Biology,* eds. M. Meltzer and A. Mantovani. New York: John Wiley and Sons, 157-62.
Hannun, Y.A., and R.M. Bell, 1991. Signal transduction and cancer. In Cancer *Medicine,* 3d ed., eds. J.F. Holland, E. Frei III, R.C. Bast, Jr., D.W. Kufe, D.L. Morton, and R.R. Weichselbaum. Philadelphia: Lea and Febiger Publishers, 48-65.
Dennis, E.A., S.G. Rhee, *M.M.* Billah, and Y.A. Hannun, 1991. Role of phospholipases in generating lipid second messengers in signal transduction. *FASEB Journal,* 5:2068-77.
Werner, M., L. Senzel, A. Bielawska, W. Khan, and Y.A. Hannun, 1991. Diacylglycerol overcomes aspirin inhibition of platelets: Evidence for a necessary role for DAG accumulation in platelet activation. *Molecular Pharmacology,* 39:547-56.
Werner, M. and Y.A. Hannun, 1991. Delayed accumulation of diacylglycerol in platelets as a mechanism for regulation of onset of aggregation and secretion. *Blood,* 78:435-44.
Khan, W.A., S.W. Mascarella, A.H. Lewin, F.I. Carroll, and Y.A. Hannun, 1991. Use sphingosine as a pharmacologic inhibitor kinase C in human platelets. *Biochemical* 387-92.
Khan, W.A., S. El Touny, and Y.A. Hannun, 1991. Arachidonic and *cis* unsaturated fatty acids induce selective platelet substrate phosphorylation through activation of cytosolic protein kinase C. *FEES Letter,* 292:98-102.
Alessenko, A., W.A. Khan, W.C. Wetsel, and Y.A. Hannun, 1992. Selective changes in protein kinase C isoenzymes in rat liver nuclei during liver regeneration. *Biochemical and Biophysical Research Communications,* 182:1333-39.
Werner, M.H., A.E. Bielawska, and Y.A. Hannun, 1992. Multiphasic generation of diacylglycerol in thrombin-activated human platelets. *Biochemical Journal,* 282:815-20.
Werner, M.H., A.E. Bielawska, and Y.A. Hannun, 1992. Quantitative analysis of diacylglycerol second messengers in human platelets: Correlation with aggregation and secretion. *Molecular Pharmacology,* 41:382-86.
Khan, W.A., G.C. Blobe, and Y.A. Hannun, 1992. Activation of protein kinase C by oleic acid: Determination and analysis of inhibition by detergent micelles and physiologic membranes;

requirement for free oleate. *Journal of Biological Chemistry,* 267:3605-12.
Wetsel, W.C., W.A. Khan, I. Merchenthaler, H. Rivera, A.B. Halpern, H.M. Phung, A. Negro Vilar, and Y.A. Hannun, 1992. Tissue and cellular distribution of the extended family of protein kinase C isoenzymes. *Journal of Cell Biology,* 117:121-33.
Bell, R.M., D. Burns, T. Okazaki, and Y.A. Hannun, 1992. Network of signal transduction pathway involving lipids: Protein kinase C dependent and independent pathways. In *Neurobiology of Essential Fatty Acids,* eds. N. Bazan, G. Toffano, and M. Murphy. New York: Plenum Press, 27584.
Dobrosky, R.T. and Y.A. Hannun, 1992. Ceramide stimulates a cytosolic protein phosphatase. *Journal of Biological Chemistry,* 267:5048-51.
Linardic, C.M., S. Jayadev, Y.A. Hannun, 1992. Brefeldin A promotes hydrolysis of sphingomyelin. *Journal of Biological Chemistry,* 267:14909-11.
Pushkareva, M. Yu, W.A. Khan, A.V. Alessenko, N. Sahyoun, and Y.A. Hannun, 1992. Sphingosine activation of protein kinases in jurkat T cells: In vitro phosphorylation of endogenous protein substrates and specificity of action. *Journal of Biological Chemistry,* 267:15246-51.
Bielawska, A., C.M. Linardic, and Y.A. Hannun, 1992. Modulation of cell growth and differentiation by ceramide*FEES Letters,* 307:211-14.
Bielawska, A., C.M. Linardic, and Y.A. Hannun, 1992. Ceramide-mediated biology: Determination of structural and stereospecific requirements through the use of *N* acylphenylaminoalcohol analogs. Journal *of Biological Chemistry,* 267:18493-97.
Hannun, Y.A., 1992. Sphingolipid-derived breakdown products: Role in cell regulation. In *New Leads and Targets in Drug Research, The Alfred Benson Symposium,* eds. P. Korgsgaard Larsen, S. Brogger Christensen, and H. Kofod. Copenhagen: Munksgaard, 33:257-68.
Obeid, L.M., G.C. Blobe, L.A. Karolak, and Y.A. Hannun, 1992. Cloning and characterization of the major promoter of the human protein kinase C p gene: Regulation by phorbol esters. *Journal of Biological Chemistry,* 267:20804-10.
Chao, R., W. Khan, and Y.A. Hannun, 1992. Retinoblastoma protein dephosphorylation induced by D-erythrosphingosine. *Journal of Biological Chemistry,* 267:23459-62.
Blobe, G.C., C.W. Sachs, W.A. Khan, D. Fabbro, S. Stable, W.C. Wetsel, L.M. Obeid, R.L. Fine, and Y.A. Hannun, 1993. Selective regulation of expression of protein kinase C isoenzymes in multidrug resistant MCF-7 cells: Functional significance of enhanced expression of PKC *a. Journal of Biological Chemistry,* 268:658-64.
Khan, W.A., G.C. Blobe, A. Halpern, W. Taylor, W. Wetsel, D. Burns, C. Loomis, and Y.A. Hannun, 1993. Selective regulation of protein kinase C isoenzymes by oleic acid in human platelets. *Journal* of *Biological Chemistry,* 268:5063-68.
Karolak, L., A. Chandra, W. Khan, B. Marks, W.P. Petros, W.P. Peters, C.S. Greenberg, and Y.A. Hannun, 1993. High-dose chemotherapy-induced platelet defect: Inhibition of platelet signal transduction pathways. *Molecular Pharmacology,* 43:37-44.
Obeid, L.M., C.M. Linardic, L.A. Karolak, and Y.A. Hannun, 1993. Programmed cell death induced by ceramide. *Science,* 259:1769-71.
Dobrowsky, R.T. and Y.A. Hannun, 1993. Ceramide activated protein phosphatase. Partial purification and relationship to protein phosphatase 2A. In *Advances* in *Lipid Research,* eds. Bell, R.M., A.H. Merrill, and Hannun, Y.A.. New York: Academic Press (in press).
Hannun, Y.A., L.M. Obeid, and R.A. Wolff, 1993. The novel second messenger ceramide:

Identification, mechanism of action, and cellular activity. In *Advances in Lipid Research*, eds. Bell, R.M., A.H. Merrill, and Hannun, Y.A.. New York: Academic Press (in press).

Fishbein, J.D., R.T. Dobrowsky, A. Bielawska, S. Garrett, and Y.A. Hannun, 1993. Ceramide mediated growth inhibition and CAPP are conserved in *saccharomyes cerevisiae. Journal of Biological Chemistry*, 268:925561.

Blobe, G.C., W.A. Khan, A.E. Halpern, L.M. Obeid, and Y.A. Hannun, 1993. Selective regulation of expression of protein kinase C p isoenzymes occurs via alternative splicing. *Journal of Biological Chemistry*, 268:10627-35.

Dobrowsky, R.T., C. Kamibayashi, M.C. Mumby, and Y.A. Hannun, 1993. Ceramide activates heterotrimeric protein phosphatase 2A. *Journal of Biological Chemistry* (in press).

ABSTRACT

Yusuf A. Hannun was born in Dhahran, Saudi Arabia, though raised after the age of five in Beirut, Lebanon, the eldest of three siblings. His father was a medical officer in the British Army during the World War II and later became a physician at the Arabian-American Oil Company (ARAMCO) stationed in Saudi Arabia and then started his own private practice in Lebanon. Hannun's parents believed wholeheartedly in education; Hannun attended the International College in Beirut for his studies. He always excelled in school and had a broad-based education with an emphasis, and an interest for Hannun, in the sciences and mathematics. He was an avid reader and a competitive swimmer, and he knew from a young age that he was going to pursue a career in medicine, even if it served as a fallback to some other area of study. Hannun began to notice political tensions within the country at the end of high school, and subconsciously decided to undertake his career abroad.

He studied medicine at the American University of Beirut, specializing in internal medicine. He decided not to stay in the Middle East and took a subspecialty in oncology/hematology at Duke University Medical Center in Durham, North Carolina, at which point he decided to focus on biomedical research. He studied the connection between protein kinase C and diacylglycerol with James E. Neidel and Robert M. Bell, after which he received a National Institutes of Health Physician Scientist Award and began his work on sphingolipids and protein kinase C while remaining at Duke.

Much of the interview is spent discussing the cultural, social, and political life of Lebanon, the civil war, and Hannun's comparison of life in the United States to life in Lebanon, and some time is spent discussing the Palestinian Liberation Organization. The interview concludes with Hannun's thoughts on labs that combine a structural and functional approach to science; the justification for doing basic research; his Pew Scholars Program in the Biomedical Sciences award; and the politics of funding. He ends with a discussion of National Institutes of Health peer reviewers; his research on protein kinase C; his family; his collaboration with his wife, Lina Obeid Hannun; and women and minorities in science.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Neil D. Hathaway, Interviewer, UCLA Oral History Program. B.A.., English and History, Georgetown University; M.A. and C. Phil., History, UCLA

TIME AND SETTING OF INTERVIEW:

Place: Tapes I-II & V-VII - Hannun's office, Duke University Medical Center.
Tapes III-IV – Hannun's Home, Chapel Hill, North Carolina

Dates, length of sessions: March 29, 1993 (104 minutes); March 30, 1993 (88); April 1, 1993 (85); April 2, 1993 (161).

Total number of recorded hours: 7.3

Persons present during interview: Hannun and Hathaway.

CONDUCT OF INTERVIEW:

This interview is one in a series with Pew scholars in the biomedical sciences conducted by the UCLA Oral History Program in conjunction with the Pew Charitable Trusts's Pew Scholars in the Biomedical Sciences Oral History and Archives Project. The Project has been designed to document the backgrounds, education, and research of biomedical scientists awarded five-year Pew scholarships, from 1988 through 1992.

In preparing for this interview, Hathaway, in consultation with the director of the UCLA Oral History Program and three UCLA faculty project consultants, developed a topic outline to provide an overall interview framework. Hathaway then held a telephone preinterview conversation with Hannun to obtain extensive written background information (curriculum vitae; copies of published articles, etc.) and agree on a research and interviewing timetable. Hathaway further reviewed the documentation in Hannun's file at the Pew Scholars office in San Francisco, including his proposal application, letters of recommendation, and reviews by Pew Scholars Program national advisory committee members. For general background on the recent history of the biological sciences, Hathaway consulted such works as J.D. Watson et al. *The Molecular Biology of the* Gene. 4th ed. 2 vols. Menlo Park, CA: Benjamin/Cummings, 1987; Lubert Stryer. *Biochemistry.* 3d ed. New York: W.H. Freeman, 1988; *Journal of the History of Biology;* and H.F. Judson. *The Eighth Day of Creation: Makers of the Revolution in Biology.* New York: Simon and Schuster, 1979.

The interview is organized chronologically, beginning with Hannun's childhood and education in Saudi Arabia and Lebanon and continuing through his education at American University of Beirut and his postdoctoral fellowship and subsequent professorship at Duke University Medical Center. Major topics discussed include the Middle East; clinical medicine; Hannun's research on protein kinase C, diacylglycerol, sphingosine, and the mitogenic pathway; and the politics of basic science funding.

ORIGINAL EDITING:

Steven J. Novak, editor, edited the interview. He checked the verbatim transcript of the interview against the original tape recordings, edited for punctuation, paragraphing, and spelling, and verified proper names Words and phrases inserted by the editor have been bracketed.

Hannun reviewed the transcript. He verified proper names and made minor corrections.

Novak also prepared the table of contents, biographical summary, interview history, and index.

TABLE OF CONTENTS

INTERVIEWEE: **Yusuf A. Hannun**

INTERVIEWER: **Neil D. Hathaway**

LOCATION: **Duke University Medical Center**
Durham, North Carolina

DATE: **29 March 1993**

HATHAWAY: Since I probably won't call you by name, I will say your name in the beginning. I'm interviewing Yusuf [A.] Hannun. [Pronounced] Hannun is right?

HANNUN: Yes. That's correct.

HATHAWAY: At Duke [University Medical Center]. I don't alter the beginning. I always simply ask where and when you were born. Do you want to start there and just talk about your family?

HANNUN: I was born in Dhahran, Saudi Arabia. My father [Awni Hannun] was a physician at the Arabian-American Oil Company, ARAMCO. We were living in sort of the town [Ras Tannoura] built by ARAMCO to house families who came to Saudi Arabia to work there. That's where I spent the first four to five years of my life mostly, as the first child. I'm four years older than my brother [Imad Hannun]. My sister [Rana Hannun Bibi] is two years younger than my brother.

HATHAWAY: So, you were the only one born in—

HANNUN: I was the only one born in Dhahran. My brother was born in Beirut [Lebanon], but he came back to Dhahran for a little while before we finally moved to Beirut. So he was born in that transition period.

HATHAWAY: And what's your birth date, just for the record?

HANNUN: My birth date is September 18, 1955. We moved to Beirut--I'm not a hundred percent sure now--in '60 or '61.

HATHAWAY: Why had your father taken the job with ARAMCO?

HANNUN: Well, my father is a physician. He was originally Palestinian, but he had left Palestine in I would think the thirties, went to Glasgow, Scotland, got his M.D. degree there and training, and joined the British army for World War II, because he couldn't go back to his country during World War II.

HATHAWAY: Because nobody would—

HANNUN: There was no transportation, basically. He joined the British army as a medical officer and spent the balance of the war-- I don't know what year he joined, but he spent several years until the end of the war with the British army, mostly in Europe. After that, I think he returned back to Palestine. That was the interphase between World War II in '45 and the partition in '48. He had to leave then as part of the evacuation, deportation, what have you, that happened, the massive exodus that happened in '48. I think at that time he went to Jordan, worked as a physician there, but then went to Saudi Arabia. So most of the fifties I think he was in Saudi Arabia.

HATHAWAY: Perhaps it was a better opportunity, perhaps even more lucrative than practicing medicine in Jordan. Was he practicing medicine in the Palestinian community there?

HANNUN: In Jordan?

HATHAWAY: Yeah.

HANNUN: I really don't know the details of that. I know for one thing he was somewhat politically involved in Jordan. We still have the same king in Jordan from the fifties.

HATHAWAY: Hussein [I], right.

HANNUN: Hussein. My father, after being in the British army, went back to the Jordanian army as a physician, and with some political discontent or something he quit that job. I think from there he went to Saudi Arabia for a job opportunity. Maybe there was some sort of political conflict--nothing serious--but something that he probably wasn't comfortable staying in Jordan for.

HATHAWAY: I realize this is more about your father, and so it really is just background. But if I understand correctly, there is a very large Palestinian population, and I believe that Hussein has been allied with them. I mean, there has always been some tension between Jordanian nationals and Palestinians, but there has always been a political connection between Hussein and his maybe staying in power or support.

HANNUN: That's a good assessment. I think it's an important question because a lot of those concepts I think are formative for me in terms of my political awareness. The funny thing about it was Jordan was carved out by the British and French after World War I. After '48 there was a massive exodus of Palestinians, so there's a big segment of Palestinians. I think now it's estimated at 60 percent or something. And then there is a 30 to 40 percent sort of the indigenous population of Jordanians, who were either tribal people or the sort of people who lived in a couple of cities there.

HATHAWAY: I guess I wasn't aware that the Palestinian population was then a majority within—

HANNUN: It is.

HATHAWAY: I knew it was a large segment, but I didn't realize it was actually—

HANNUN: Yeah. It is a majority. The funny thing about it, though, is the king is not one of those indigenous Jordanians. The king comes sort of from the Arabian peninsula lineage that he traces all the way back to the prophet Muhammad. Again, between World War I until World War II, that family has-- I forget the lineage. His uncle was prince of Iraq [Faisal], and his grandfather or his great-grandfather [Hussein] tried to establish sort of an Arabian kingdom between Syria and Jordan and Iraq. And then his son [Abdullah] became king of Jordan and the other son [Faisal] king of Iraq. Hussein inherited his kingdom from his grandfather as a very young person. And he's survived since then, which is pretty remarkable for the Middle East. The king has sort of always balanced all kinds of opposing forces. There's a lot of intermarriage between the Jordanians and Palestinians. So now it's very difficult to distinguish, I think, subpopulations there, except that there are the different kinds of Palestinians, as we talked about the other day briefly, in Jordan as well as in Syria and in Lebanon and probably in Egypt. These are the countries where most of the Palestinians sort of immigrated to after '48. I think from my understanding, the Palestinians who were not endowed with either special skills or education ended up in the refugee camps, where they still are. That defines sort of one population of Palestinians. And then another population, of either the educated or people who had skills to promote, defined a very active work force, usually a highly skilled work force,

because the Palestinians apparently were and remain the most educated population in the Arab Middle East. A lot of the business people, the finance people, the physicians, the engineers in Lebanon, Syria, Jordan were Palestinians. So there is that population. That population, I think, mixed much with the Jordanian population in Jordan, mixed somewhat with the Syrian population, probably to a lesser degree with the different Lebanese populations because Lebanon tends to be more strictly defined along ethnic or religious background.

So that's sort of my father's background. I think the main reason he went back to Saudi Arabia is I think he was politically unhappy with Jordan at that time aligning with Iraq and what was the Baghdad Pact. And his being in the military, sort of, I think he resigned and just left the country.

HATHAWAY: That perhaps his own political views were known and he would no longer make it any further or would be in a very uncomfortable position, anyway.

HANNUN: Probably something like that. I don't think he was in danger of being imprisoned or hurt, but I think he was just not comfortable with being part of it, I guess.

HATHAWAY: Do you know how he became involved in this? Do you know whether it was through his involvement in the war, let's say, in Europe and through British connections? Or do you think it was from family connections and his growing up in Palestine?

HANNUN: I think the latter, much more the latter. think his sort of experience in the Second World War enabled him to assume a top position in the medical branch of the army in Jordan because he was sort of uniquely qualified for that position. But I think his sort of political activism, in retrospect, like many of his generation, was very naive and very impulsive and was shaped a lot by the events that were happening in Palestine over the thirties and forties and whatnot. People just didn't comprehend what was going on in terms of the creation of Israel, the support of the West for that, and sort of the major friction that arose between the West and the Arab Middle East. I think a lot of that resentment and sort of denial led to very naive political activism that pretty much led nowhere. That's obviously in retrospect. I think those were the greater motives for that.

HATHAWAY: And as you say, your family moved back to Beirut when you were—

HANNUN: Approximately five years of age.

HATHAWAY: So that really to talk about Dhahran beyond perhaps one or two very vague

memories is really not—

HANNUN: Yeah. I have some happy recollections of Dhahran. I don't know whether it was the atmosphere there, being the only child at that time. I think jobwise my father was in a very good position. I think he was the director of the hospital there, too, for ARAMCO.

HATHAWAY: And so this would have been a hospital for any type of foreigner, in other words, American, British, and other Middle Eastern.

HANNUN: Most of the foreigners who lived in-- Actually, it's not Dhahran. It's called Ras Tannoura. It's where the refinery is. From my recollection, it's like regular suburban USA, you know, individual homes with a little garden and then a supermarket and all that transplanted there. I do have some recollections of our neighbors. One family was a physician from India. Another family was-- God, I forgot. Definitely a couple of American families there and one with kids my age. I remember those somewhat vaguely too. So these are my recollections of that. They were happy years, I think, but I have a feeling that my parents didn't want to bring us up in that environment.

HATHAWAY: For what reasons?

HANNUN: Maybe for sort of-- I don't want to say political, but maybe social reasons. They didn't want us to grow uprooted, basically. I mean, it was predominantly an American cultural impact there. That I think became quite an obvious concern for them--that I was growing up with English as a first language and not being part of an Arab culture.

HATHAWAY: You say English was your first language, obviously was spoken everywhere outside of your family. But I take it you were speaking Arabic at home. Although your father, of course, was, I'm sure, more than fluent in English.

HANNUN: I would say at home it was mostly Arabic, but then because it was such a close neighborhood, the common language was English.

HATHAWAY: And your mom [Aida Ashour Hannun], where did your father meet her or what was her--? I mean, she spoke English, too, then, I take it.

HANNUN: Yeah. My mom was also of Palestinian origin. Her family immigrated to Lebanon

in ‘48, and that’s where she went to high school and college or maybe just college. I forget if she had finished high school before ‘48. They got married in the early fifties. I think it was more or less a prearranged-- Not prearranged but sort of through mutual friends that my father was introduced to my mother and they got engaged and then they got married. And then my mom went back to Saudi Arabia with my dad. I think the choice of Lebanon over Jordan was dictated by, one, I don’t think my father still wanted to go back to Jordan at that time, and [two] my mother’s family was all in Lebanon. So they decided to go to Beirut at that time.

HATHAWAY: And your father’s family, had they--?

HANNUN: If you want to get back into that kind of history, it’s—

HATHAWAY: Not perhaps in great detail but just a sense of how-- Because of course everybody was uprooted.

HANNUN: It’s funny, because the roots of my father’s family are in a town called Tulkahrm, which is in the West Bank, with my grandfather [Yusuf Hannun]. They were sort of landlords and things like that, and my grandfather was their, I guess, export-import connection. He was located in Jaffa, sort of the port of Jaffa. So that’s where he established his own land and property and residence. That’s where my father and all my uncles and aunts grew up. And very analogously, my maternal grandfather [Yusuf Ashour] was originally from a West Bank town called Nablus. Again, he was located in Jaffa for similar reasons, because both families apparently were landlords with a lot of orange groves and what have you. The immediate families were translocated, but the rest of the extended families are still in Tulkahrm and Nablus. My mother’s family went to Lebanon rather than go to Nablus. I think the only way they could leave Jaffa was by sea at that time, so that’s why they went that way. But my father’s family went initially to Lebanon but went back to Tulkahrm, so they stayed more in the West Bank.

HATHAWAY: Again, I think this is important. You mentioned actually a few things. I’m just kind of guessing at this or suggesting that maybe this is some way of understanding it, even for just myself so that this conversation can flow more easily. I don’t want to--Well, it’s not so much a class distinction, but you mentioned the fact that, for instance, quite a large portion of the Palestinian population became refugees. They really were not wealthy enough or were not recompensed because they didn’t have property. I don’t know exactly what happened. There seem to be two cultures, let’s say, or something like that, within the Palestinian culture. For instance, this arranged situation between your parents would come from a pretty close-knit and maybe small—

HANNUN: I think it came about because both families grew up in Jaffa, so they had a lot of mutual friends.

HATHAWAY: This isn't such a planned or traditional way i of doing things in Palestinian culture.

HANNUN: No. I guess my dad wanted to get married, and he was asking around. I would think he wanted to marry a Palestinian lady. And because of his friends and both families growing up in the same town, that's how it ended up being.

HATHAWAY: And you mentioned you father-- When they left Saudi [Arabia], there was no place to go back to. Going to Lebanon and Beirut, there was a choice over perhaps Jordan or maybe even other places. Was there a job there? You mentioned there was some family there, your mother's family. It was just time to get out of Saudi Arabia, perhaps, and this kind of artificial American culture.

HANNUN: I think, yeah. I must tell you that a lot of the decision making there has not been-- You know, I wasn't part of—

HATHAWAY: And you didn't ask.

HANNUN: Yeah. Maybe also part of leaving ARAMCO was the fact the job wasn't going anywhere or something. I really don't know the economic or financial aspects of those decisions. The first few years in Beirut my father started out on his own as a private practitioner. He chose a clinic very close to Palestinian refugee camps so he could sort of cater to that group of patients, and he stuck to that throughout the remainder of his career. He did take an additional job with the UNRWA [United Nations Relief Work Agency], which is the relief agency for the UN that caters to Palestinians. So he had sort of dual—

HATHAWAY: A private sort of practice and also-

HANNUN: A private practice and that, but both were heavily catered towards serving Palestinian refugees.

HATHAWAY: That may indeed be the answer to the question about why Beirut or why Lebanon, because certainly as far as I can tell the problems for refugees and the situation for

Palestinians was more acute in southern Lebanon than elsewhere, perhaps, or than even the West Bank, at least economically.

HANNUN: Oh, yeah. At that time the West Bank was a very integral part of Jordan, so there was no discrimination at all. The Palestinians who could make inroads into the productive strata of society in Jordan were automatically admitted on equal footing, the same in Syria, with a little more difficulty in Lebanon. But, again, my father could easily set up practice there. The obstacles couldn't have been very formidable.

But there has been a political [force], I think, also, a political and not just an economic force creating those refugee camps. The delicate balance in Lebanon would not have taken admission of a refugee community into it, which would have tilted the balance, the religious and ethnic balance. I think also, in a more global political sense, there was a feeling that this refugee problem was very temporary, because even when I left Lebanon in '83 they still lived in tin shacks, you know, temporary, even though they've been in it for more than—

HATHAWAY: Temporary, but where were they going?

HANNUN: I think there was strong feeling that they were sooner or later going back to Palestine. And obviously the political leaders were reinforcing that day and night, although without the ability to deliver on those promises. Maybe there was also a deliberate, initially subconscious, but maybe more articulated decision on the part of Arab governments to keep the refugee problem rather than assimilate Palestinian refugees. I mean, not just sort of not to create imbalances. That was one factor, but another factor was to maintain that as a status quo. Irrespective of the perception of Palestinians and many others that this was temporary, I think the governments wanted as more a political expediency to keep it as an ongoing problem.

HATHAWAY: Sure. And indeed it is, right.

HANNUN: And it is, yeah.

HATHAWAY: I guess maybe this is inappropriate to ask you with retrospect and hindsight. I mean, you experienced it, and now you've had some distance from it. I'm not asking you to kind of recreate how you thought about it then but I guess how you think about it now. Given that in many ways the situation is still, quote, "the same," although things do change slowly and there always seems to be a chance in the foreseeable future some settlements and agreements will be made such that there will either be two nations or there will be some-- What was your sense, when you were growing up, of what was going on around you? Was it a sense of, yes, someday your family or maybe you yourself would be able to go back to where your family's

roots were?

HANNUN: That's a very loaded question.

HATHAWAY: I know, so take your time. That's probably five or six questions, and I really don't want to narrow it or define it so that you have to answer one of them.

HANNUN: I think all that background has been very formative for me.

HATHAWAY: Yeah. You mentioned that. That's what I'm trying to get a sense of.

HANNUN: In one way, I think the '48 exodus has reinforced in a lot of Palestinians' minds, and especially my family's, that education was their salvaging, redeeming point. Education was always the highest priority in our family, no question about that whatsoever. So much so that in retrospect my parents initially prevented us from engaging in any activity that could remotely take us away from education.

HATHAWAY: So no playing in the afternoon. You came home and—

HANNUN: Not really. That was temporary because I think my brother, sister, and myself did sufficiently well--very well--at school that we bought our freedom, so to speak. But earlier on, especially with me, I was the one most restricted to sort of give up other things, whether it was piano lessons or whatever. But as we proved ourselves, so to speak, and showed that we could deal with school and education, we bought our freedom. So in high school and whatnot—

HATHAWAY: As long as you brought home good grades.

HANNUN: There was no problem whatsoever. Actually, the funny part is education was so much emphasized that almost nothing else mattered. I could do whatever I wanted to do as long as my grades were top-notch.

HATHAWAY: So it wasn't that you needed to learn how to play the piano, if that's what you wanted to do, or play tennis-- You know, I'm just picking things out of the air.

HANNUN: There was no attempt at religious education. There was no attempt at even modifying my behavior as a teenager, which at times, in retrospect, was probably quite nasty.

HATHAWAY: We'll get to that.

HANNUN: Education was an overriding concern. The other thing, the political awareness, growing up in Lebanon, unfortunately-- I don't want to say "unfortunately," but definitely a distinctive feature of it is, because of the sort of strict ethnic and religious identification of people in Lebanon, you could almost recognize by a person's name where they come from and what religion they belong to. I don't know if you can sort of imagine how such a society would interact with a foreigner, which I was basically. I was not Maronite; I was not a Druze; was not Lebanese. So I was never totally molded by or taken by the Lebanese social structure. I want to bring that up because it's extremely different from the U.S. culture. Because in the U.S., it's such a melting pot that it doesn't matter where you come from. It depends on who you are. In the Middle East, it's almost the reverse of that. It doesn't matter who you are but where you come from. The closest thing sort of to that in the U.S. would be, what was it, East of Eden.

HATHAWAY: The movie, right, yeah.

HANNUN: The novel by Steinbeck. In terms of how a foreign family or family from the outside comes in and integrates and how that shapes the development of the family.

HATHAWAY: Our history is almost wave after wave of different kinds of immigrants finally assimilating, you know, the third generation or second, from Europeans, western Europeans, over a century ago, to Asians.

HANNUN: Yeah. It's very mixed. You really care here much more about who the person is. So in Lebanon, going back to your political question, I could always sense that I was different, because I was considered a little different. I'll grant you that there were many ameliorating factors to that, so I never felt rejected. It's not a feeling of rejection because there were-- I am Sunni Muslim, so I could be considered part of that.

HATHAWAY: Even among Muslims in Lebanon, right, the Shiite—

HANNUN: The Shiites now are the majority. Back then, who knows. I mean, definitely the Sunnis had more political clout. There were many other Palestinians, mostly maybe Christian but also some Muslim, who were in sort of a similar situation. So there were other kids in my

school with similar backgrounds. I wasn't really an outcast or rejected. I was just different. I wasn't Lebanese.

And there was always this question of what's going to happen to Palestinians over time, this uncertainty. That was obvious at home. I grew up with that. As I mentioned before, [there was] the expectation that pretty soon we'll be going back. The turning point came, at least to me, in '67, when there was such a hype built up by [Egyptian President Gamal Abdel] Nasser that "Hey, that's going to be solved." We were going to confront the Israelis and the French and whatever and just solve this problem. In retrospect, it looks like he was totally suckered into it, and overnight reality hit home. I was only, what, eleven, at that time. Reality hit that that kind of political demagoguery wasn't going to solve the problem, that the problem was much more fundamental than that.

HATHAWAY: Was this also a point of realization for many Palestinians, that Israel was perhaps more--?

HANNUN: Stronger in the long term. Yeah. It wasn't a temporary wrinkle in the history of the region, you know, like no Israel for two thousand years and then there is going to be no Israel for the next two thousand years. It wasn't a wrinkle. That was a reality to be confronted. Although I would say at the population level that did not go much further than that in terms of-- "Okay, that's a more severe case than we thought," but it didn't translate into "Okay, well, let's see how we can solve it and deal with it." Obviously, the Israelis at that point, at that time, didn't want to make it any easier, either, by coming out victorious. At first [Israeli Prime Minister] Golda Meir said, "Who are the Palestinians?" I mean, they were not in the mood of accommodating at that time. Therefore the reaction was the growth of the Palestinian radical movements and the armed resistance movement. That was a direct outcome of the 1967 war. But to me it was an eye-opener that the infrastructure to deal with the aspirations of Palestinians or Arabs was just not there. It wasn't a mere change in leadership or the political program. The education wasn't there, the understanding wasn't there, of how to deal with the situation. I mean, until '67, people were in the mind-set of, "We're going to ignore this problem until it goes away." Basically refusing to acknowledge that Israel exists. I mean, other than what you hear about in terms of Arab states not recognizing Israel. That's a political maneuver. But even at the level of people refusing to hear Israeli news or acknowledge that Israel existed-- It was a nightmare that was going to go away. After '67, this nightmare was not going to go away. But the reaction was still very immature in terms of how do we deal with that. And as I said, the Israeli political system at that time wasn't in any compromising mood either, so it just resulted in armed conflict.

HATHAWAY: One other area in kind of asking a rather, I guess, undefined or series of questions in one question--Certainly on this political level and your awareness of it, it must have been quite striking for an eleven-year old-- I mean, really, although, again, you've got the hindsight of being an adult and other events happening to be able to filter those feelings and emotions through. I also was hoping to get some sense of the community you were in, and for

yourself those kinds of experiences, like somebody at school and things like that. You mentioned when we met last Friday, just kind of got acquainted, that although it was a small part of Beirut, there was a part of Beirut where everything was mixed, where it didn't matter what your religious background and your family background or ethnic background was. assume that this also was true maybe in school and on the streets and in the cafe. I mean that this was-- I'm wondering.

HANNUN: Yeah. That's definitely true. I mean, I grew up in what's called Ras Beirut. This is sort of like a peninsula to the west of Beirut surrounded by the Mediterranean on pretty much three sides of it. It's really centered around the American University of Beirut and the hospital of the university. The school I went to [International College] was an offshoot of the American University and was structured very much the same way, run by an American board of trustees out of New York. The president was American. Invariably, most of the senior administration was American. It was a very, again, by relative terminology, liberal education and totally nondenominational. The whole area of Ras Beirut was very unique, very cosmopolitan, when I was growing up. Beirut was the financial capital and the intellectual capital and the political capital for the Middle East, basically, and a very good interface between Europe and the rest of the Middle East, especially at that time when the oil-rich countries were starting to want access to the West. Really, Lebanon was at the interface of that. Usually when you say Lebanon, it's Beirut, and when you say Beirut, it was really that segment of Beirut. So that was sort of the central nervous system of the whole operation there.

It was very cosmopolitan, very mixed. I think in terms of Lebanese it was equally mixed, you know, Christians and Muslims. As I told you the other day, the Christians in Ras Beirut didn't leave during the civil war. So it was a very tolerant, mixed population. There were a lot of the Palestinian class of educated Palestinian people. When I went to school I had all kinds of friends from all sources, all facets of middle-class Lebanon, or middle- to upper-middle-class Lebanon. It resulted in a very interwoven social fabric, because when you grow up with one group, one cohort of classmates, and their brothers, ancestors, families, and other acquaintances, you get to know directly or indirectly almost everyone there, which is a very sizable number.

HATHAWAY: Would you care to give a rough estimate? I mean, we know this is not exact.

HANNUN: I would say it's in the several thousands.

HATHAWAY: And they would know who you were, again, just simply by some sort of, "Oh, that's so-and-so's son," right, even if they hadn't ever—

HANNUN: Exactly, exactly.

HATHAWAY: And this is, again, you say Christian and Muslim and Palestinian and Lebanese.

HANNUN: Yeah. I mean, you could easily make all those associations. Like if someone didn't know my parents, they may know who my aunt was married to or their family. You could almost immediately, when you were introduced to someone, find common acquaintances or even relations. And this very extended social fabric is very different than what you have in this country, very different. bring it up because I can see how Americans cannot see that. It's extremely different. I mean, Ras Beirut was bigger than Durham [North Carolina], yet I probably know one-hundredth, relatively, the number of people in Durham. The social interactions were different. I mean, if you went to the gas station, in a year--because things don't change, things don't move--you get to know those people and you know the people they know and the same about the people who run a restaurant and the people who run a store. You get to know those people at a personal level too. So the social fabric was very different.

HATHAWAY: Is this something that you still have? I mean, even given all that's happened in Beirut since-- I mean, now we're talking about your going to school at perhaps even kind of what we would call in this country junior high or high school. We're talking up into the end of the sixties and well into the seventies, I assume. Things changed quite a bit even at that time but then certainly since, even before you left in '83, but there is still this kind of-- What's the word I'm looking for?

HANNUN: Do you mean does it still exist or is it in my consciousness? Which are you implying?

HATHAWAY: I guess maybe I'm asking about both. But let's pick one, let's say your consciousness, something you miss and wish that your children would have here.

HANNUN: Yes, absolutely. It's something I miss. It's something my wife [Una Obeid Hannun] misses, because, although she's American-born, she grew up pretty much in the same environment. I don't know if I wish it on my children [Awni, Marya, and Reem Hannun] or not. I would have liked for them to be sort of part of that. It's a very difficult question what to wish for your children. I think it's a trade-off. I think from my philosophical sort of analysis of it, I think it's a trade-off between trying to foster excellence and matching the best person for the best job and having mobility and therefore negating roots, or having roots and trying to find the best job any one person can do rather than match the best person. So you sacrifice one for the other. If you want to maintain roots, you don't foster excellence and achievement. I sort of believe in that.

HATHAWAY: That's something that you've come to realize, let's say, for instance, from your

own career or your own experiences now as a biologist and somebody who is actually running quite a-- We'll call it an operation. don't mean to be glib about it or flip, but it's quite an operation that's going on here [Duke University Medical Center], and you are in charge. And so obviously you're looking for people who perhaps think the same way, too, who are for instance willing to move to Durham and would never have any connection to their own—

HANNUN: Exactly. They move because they think this is the best thing for them.

HATHAWAY: And I take it's that's why indeed you're here in Durham still and not back in Beirut.

HANNUN: Yeah. Exactly.

HATHAWAY: Or maybe even why you left originally to come here.

HANNUN: Yeah. That's a pretty much accurate assessment.

HATHAWAY: I guess the other question just for historical purposes or for the record, because we have somebody whose experience is so tied up with it-- What is left of this, again, I guess, the part of Beirut? I don't want to try to pronounce it.

HANNUN: As Graham Greene once said, "A city without its people is a collection of concrete and steel." I think that's what's left of it. Most of the people who could have left have left, basically. They're all over the world.

HATHAWAY: Especially from the Palestinian point of view, again, maybe, one more exodus.

HANNUN: For the Palestinian, it was one more exodus; for the Lebanese, it was a new one, yeah. Many of them are all over. Because that's what happened in a more global sense in the Middle East. The people who want to concentrate on their own abilities and to achieve and move on with it, I mean, they're always constrained by all this political, not just the fighting but all the constraints that developed from that. I see it happening in Lebanon among the Palestinians, also among the Israelis. It's sort of a sad twist to the thing, because you're sort of depleting the area of the people who would be much more open-minded and tolerant and leaving in place the people who are less tolerant.

[END OF TAPE 1, SIDE 1]

HATHAWAY: You kind of maybe got to an endpoint on a topic. I would like to still pursue a little bit more, I guess, your education, a sense of the milieu in which the education happened, but perhaps more along the lines of curriculum, especially perhaps as things loosened up and you were able to do more things, your parents weren't sitting on you saying, "Study, study, study." If that's something you want to pursue, perhaps with the aim of why it ended up in med school or ended up at American University in Beirut or something like that.

HANNUN: The school I went to, incidentally, is the International College. Again, by American standards it had a very rigid curriculum, not much flexibility. I mean hardly any electives. It was forced to comply with the curriculum of the Lebanese baccalaureate for high school. This was a standardized test. But the attitude was very pro education rather than pro instruction, which I cherish a lot, basically. I had many, many outstanding teachers who made education fun rather than a chore.

HATHAWAY: So you mean the emphasis was more put on investigating things as opposed to "These are the seventeen parts of grammar you need to know."

HANNUN: No, not quite that. No. That was a shortcoming of the system. Not just at the International College but definitely throughout the Middle East, there is no emphasis on inquisitive sort of scientific experimental approaches. Maybe it's very entrenched in Arab history. It's much more analytical than experimental. They did a tremendous job a thousand years ago in translating the Greek and Latin. Actually, they preserved it for the West, and they analyzed it ad infinitum, basically.

HATHAWAY: And it was their analysis, really, more than anybody else's. It was translated into Hebrew and then of course into Latin. Then it wasn't even so much Aristotle's texts that were important but of course the commentaries that went with them.

HANNUN: Yeah. So that's through Spain, through that connection. But definitely growing up, there wasn't any emphasis-- Actually, there was some downgrading of the experimental attitude. The teachers were a very respected class of people, and they definitely enjoyed what they were doing. I think the International College probably recruited by far the best teachers available. Those people were stimulated by what they were doing, and they definitely transmitted that. But I'm trying to dissociate that from the experimental attitude or lack of--

HATHAWAY: It's almost more of an attitude of the way they taught that was infectious or that got you-

HANNUN: Yes. Yeah, exactly. My problem with the educational system is, as we got closer to the Lebanese curriculum, which is sort of the equivalent of the high school program in this country, it became very mundane, very boring, and that became almost anti-intellectual. I mean, now that I think about it, there were options whether to take mathematics or literature or some other aspects towards the end of high school. I took sort of the mathematics route, but I had occasion to look at what they taught in biology and other things that I did not take. They were literal translations from like 1940 French texts. That was mandated pretty much by the government. So it was horrible, pretty much. But what I did was sort of use that to study a lot on my own. I relied heavily on American high school textbooks in the sciences.

HATHAWAY: And these you went to a library and got?

HANNUN: Yeah. The high school library would have them.

HATHAWAY: So they would have the other texts.

HANNUN: Yeah. I definitely vividly remember the biology texts, physics texts, mostly biology and physics and chemistry.

HATHAWAY: And we're talking about textbooks. I mean, I could pull out my [Lubert] Stryer's Biochemistry, or are we talking more also like essays on evolution? Were there also that sort of--?

HANNUN: Both. Definitely the textbooks, plus additional material. I got to be very much enamored by mathematics and physics, sort of theoretical physics at that time. That for me was going to be a definite career option, to go more into mathematics.

HATHAWAY: Who did you talk with about this? Were there other students, colleagues?

HANNUN: Nobody.

HATHAWAY: Your father wasn't sitting there saying, "You're reading biology. That's great."

HANNUN: No.

HATHAWAY: Your father wasn't doing this himself also, maybe keeping abreast of medical--?

HANNUN: My father kept up with more clinical [literature], because he was really into practice, but not with sort of the basic sciences of it.

HATHAWAY: Where do you think the math and theoretical physics and all that--?

HANNUN: Came from?

HATHAWAY: Yeah.

HANNUN: Oh, I never thought of that. There was definitely an emphasis growing up, I think, that the sciences were to be coveted over-- But, again, not the attitude of the experimental aspect of science as much, think, as a selection process, that people who make it in the sciences are the smarter people and therefore they can succeed. That's why every mother wanted her children to be, at least in Ras Beirut, very good in sciences and mathematics. So there was this undertone there.

HATHAWAY: And just the general, as you said, pressure, which lightened up as you got older and you did better in school.

HANNUN: Oh, I mean, that pressure let up since I was ten or eleven.

HATHAWAY: But still in the back of all, perhaps, the influence one's parents have or the attitudes that they display toward their children and in communicating to their children what they want from them, perhaps it was the science.

HANNUN: That may have been part of it too. I think a lot of it, come to think of it, came from the literature, which showed me-- When I was even ten years old, I had a teacher who encouraged me to join the British [consul]--God, what do you call it now? Sort of the cultural attaché part to the British embassy. They had like an open library that you could subscribe to.

Even when I was ten years old, I would spend the summer going there almost daily, picking up books and reading them. That was at the sort of very elementary level. I was in elementary school. And then in high school I had a couple of American teachers who-- They used to have a program where the American teachers, you know, fresh graduates basically from college, would go spend a year in Beirut and then at the International College, teach a couple of advanced courses in usually English literature or something. That was a very small group of students, like we were three from my class.

HATHAWAY: And this was also this age, this ten, eleven, twelve?

HANNUN: No. This is past that, more like fifteen, sixteen. We went real deep into English literature.

HATHAWAY: I was going to say, you were citing Graham Greene earlier.

HANNUN: Yeah. We read that way back then probably.

HATHAWAY: Were you reading novels from the British?

HANNUN: We were reading novels from Kafka, Mann, Hermann Hesse. We read Shakespeare, a lot of Shakespeare. It was an eye-opener for me in terms of how you can access education on your own, because there was the regular curriculum that the other students were having, which was very dull and boring, and then there was this curriculum that we pretty much designed on our own. You know, "Go find a novel you want to read and discuss it tomorrow."

HATHAWAY: Kind of like an honors class or more formal?

HANNUN: It's something like that, very informal. Actually, we used to meet in the lobby of the dorms there or somewhere else. There were just two or three from my class.

HATHAWAY: Was this organized, though, by the school or by these teachers, or was this something that maybe even some of the students had way back when or sort of set up?

HANNUN: I don't know who had set it up, but it was an ongoing program where--

HATHAWAY: You knew about it before you got to the age or something--

HANNUN: Yeah. At that time, it was a really healthy program. I know the teachers who went from here just loved it because they had very flexible time and they were doing something usually they enjoyed a lot, taking those advanced or honors-type classes.

HATHAWAY: Sure, and had students who were perhaps eager and the motivational aspect didn't need to be practiced or taught. It was just the stuff itself.

HANNUN: Yeah, exactly. But it did show me that you can access knowledge and education on your own, and you can pretty much do it, because that was a definite deviation from the norm that existed there. I must have picked up on that, now that you ask the question, because after that year, that's when I started reading the sciences and mathematics on my own. I got a lot into the history of mathematics and physics. I was really taken by mathematics and theoretical physics.

HATHAWAY: And, again, no explanation or no sense of why there was the math--? I mean, we are talking about really a specific kind of knowledge, which is highly abstract, and, if you will, actually very much divorced from the kind of experimental work that you do now.

HANNUN: Absolutely. It's something I've never figured out. It used to excite me a lot.

HATHAWAY: It's not a trick question. It's actually a very common-- Not that I look for these things. You know, you [Pew scholars] all have the same background or the same thing. But it's a very common occurrence that the initial interest and the area that people do very well in-- biologists, sometimes the people I've interviewed and the Beckman [Institute] interviews-- It's very strange. It's always mathematics. And there is some point at which it's rejected for being highly abstract and having nothing to do with the world. But it seems to be the math, not physics, not chemistry, but mathematics.

HANNUN: Yeah. Mathematics was like my love in high school, and I got to be real good at it. I mean, I didn't drop it until I went into medical school. Because even as an undergrad I had to take again a fixed curriculum to enter medical school, which I had decided on, but I also majored in mathematics, side by side. I was pretty much carrying double the load of everyone else. Mathematics to me was like just go to class and that's it. I didn't even have to do homework or anything. But I had to drop that once I entered medical school. That's one reason I was very miserable the first year in medical school.

HATHAWAY: Why the choice of medical--?

HANNUN: Yeah. Why the choice of medical school? I think—

HATHAWAY: In other words, at the sacrifice of what you loved the most. I mean, you really gave it up, and it made you—

HANNUN: Yeah. Many reasons. It was many, many reasons. I guess it's one of those career choices one makes. By that time, by the time I was finishing high school, I was sensing trouble in Lebanon and friction was building up.

HATHAWAY: And we are talking—

HANNUN: In '73, '74, and you could sense trouble. There was even now starting to have polarization at my high school. [It was] very funny, because that group was like very homogeneous until the last year I was in high school, and then they started polarizing real bad.

HATHAWAY: Over what issues?

HANNUN: Over the same political issues that resulted in the civil war. I think you'll find more than one person say that what happened in my high school and in the university contributed quite a bit to the escalation towards the civil war. I don't think it ignited it or anything, but it was definitely a telling sign.

HATHAWAY: An intellectual underpinning or something of it.

HANNUN: Something like that. But even the highly educated people exposed most to other kinds of people basically got polarized. So I could tell that politically Lebanon was becoming very unstable and I couldn't plan on a career in Lebanon. That was becoming quite obvious.

HATHAWAY: Was this something you talked about with friends or your father or your mother? I mean, was it just something you kept to yourself?

HANNUN: Something I probably never articulated that way.

HATHAWAY: Something that you saw later that you were getting ready for.

HANNUN: Yeah. Something I sensed but I may have never articulated. I definitely didn't discuss it with my parents. They let me make all those choices on my own, basically. So that was one reason to avoid more questionable careers. I mean, I really believe—

HATHAWAY: Like an artist or a mathematician.

HANNUN: Yeah. You know, I told you I was very interested in the history of mathematics. Two things I learned from that influenced my career choice: one was that to achieve in mathematics or theoretical physics you have to be very fully supported by society, basically. I mean, you have to have a very stable society, a healthy society, a wealthy society, too.

HATHAWAY: What were you studying the history--? What were you equating? What were the situations or the cultures that you were looking at in the past that were giving you--?

HANNUN: Mostly looking at European physics.

HATHAWAY: I think of theoretical, right, and I think of the twentieth century.

HANNUN: Yeah, nineteenth and twentieth century.

HATHAWAY: Of prewar Germany. But I also think of the development of it in the United States as under duress, almost, and with biology, actually, people uprooted and in places where they must have felt-- You know, when I think of someone like [Salvador Edward] Luria at Vanderbilt [University] or—

HANNUN: At Vanderbilt. [Max] Delbruck and Luria.

HATHAWAY: Right. But Luria was the one who was in Nashville.

HANNUN: Yeah.

HATHAWAY: But again, so I think of it maybe perhaps as both very stable-- It's interesting that—

HANNUN: I don't think anything in the U.S.-- I mean, instability in the U.S. itself? Or in Europe?

HATHAWAY: No. I mean more these people and their sense of themselves and what they were doing in the States all of a sudden.

HANNUN: No matter where you come from, once you hit the U.S. you feel stability.

HATHAWAY: Especially the more brilliant, already established—

HANNUN: I mean the kind of instability there, which I think was validated by the events. So that was one reason. The other thing I learned from [the history of mathematics]-- I'm not sure if that's a true assessment or not, but I sort of came to the conclusion that mathematics was really a career or maybe more like a hobby for the very young. I really believed that all those people who made brilliant discoveries in mathematics or theoretical physics were pretty much done by the age of twenty-five.

HATHAWAY: It's a common belief.

HANNUN: And all those sort of misleading pictures of Einstein as an older man, discovering the secrets of the universe, are so misleading, because he was less than twenty-five when he came up with the general theory of relativity, not to mention the specific theory. So I was very disillusioned with that because I saw myself having wasted so many years in high school not developing those skills to the level I wanted and then I didn't have much opportunity in the university to develop them sort of creatively. Didactically, you could learn all what there is to—

HATHAWAY: You just weren't in the right place, perhaps.

HANNUN: Yeah. And I did learn that. I took all those courses, and I got to learn all the matrix

algebra and calculus I needed to formally, but there wasn't any room for creativity. So I think I was in the wrong place at the wrong time. And at that point, I did consider coming to the States to study mathematics. I actually sat for the SATs [Scholastic Aptitude Test] in high school. scored very high on those. I guess a couple of places offered me—

HATHAWAY: It's within a mathematics department, as well? You hadn't started looking at medical school here or--?

HANNUN: No, no. It was mathematics or economics. For some reason I also looked at economics.

HATHAWAY: They use a lot of mathematics, depending on the economics department.

HANNUN: Yeah. Theoretical economics.

HATHAWAY: Do you remember where?

HANNUN: One was the University of Chicago. And the other for the life of me I can't remember, but definitely Chicago, because I considered that very seriously. I agonized over it. I think I was young, and it wasn't the norm then for people to leave home at seventeen or eighteen, so I didn't do it.

HATHAWAY: Were a lot of your friends and colleagues also going to the American University in Beirut? I mean, was this also a community kind of--?

HANNUN: It was pretty much. It was sort of the best you could do if you stayed in the Middle East. It probably still is. With all the trouble, it's probably still a true statement. So mathematics became less and less of an option as the years went by, primarily maybe because I was in the wrong place at the wrong time.

HATHAWAY: You had only like three years left before you had to do it, right?

HANNUN: Yeah. Right. Exactly. In retrospect, I sometimes wish in high school I could have taken off two years and just studied mathematics, you know, abstract, theoretical mathematics. It's something I don't regret, but if I had to do something, I would have wanted it to be that way.

HATHAWAY: I guess you talked about reading a lot, not just mathematics but maybe we should use that as an example, again, of getting a sense-- You also noted--now at least, and looking back on it perhaps you did as well at the time--that not a whole lot of your friends and colleagues were doing this. I'm sure there were probably other people who would spend a lot of time in the library, but this is kind of a systematic, it seems, approach to the thing--"Go find every textbook on mathematics." You said you were interested in the history of it as well, perhaps not just to find out more about the content of mathematics but how it develops. And you came to some pretty actually-- What word do I want to use? Not advanced but shrewd conclusions about the development and history of mathematics from reading these things. It takes a little bit of work and quite a bit of energy to come to these kinds of conclusions. You already had this kind of mentality of looking at it from this historical perspective. What were you reading? Was there something, two or three texts or whatever, that really grabbed you? Or was this just a general kind of ongoing process that now it would be hard to dissect like that?

HANNUN: I had sort of broad-based interest in mathematics and its history. I was most captivated by Georg Friedrich Bernhard Riemann, Gauss, Leibniz, Poincare. You know, late nineteenth, early twentieth century mostly, but even earlier nineteenth.

HATHAWAY: I guess you were reading Leibniz in English?

HANNUN: Yeah, in English. Evariste Galois.

HATHAWAY: Just about everybody. You've just gone through the list. I mean, you've left out maybe--now I can't come up with his name--Fourier, but that's about it.

HANNUN: Fourier. A couple that were very impressive were Evariste Galois and the Indian guy—

HATHAWAY: I can't even pronounce his name, but I know who you mean.

HANNUN: You know who I mean, the guy who trained with Harvey.

HATHAWAY: I have trouble even pronouncing the name. When I see it I recognize it.

HANNUN: You know who I'm talking about. Galois died when he was nineteen or something, and this guy died when he was twenty-something. [Ramanchandran] I was impressed by their achievement basically a lot and by their thought process.

HATHAWAY: Maybe age identification.

HANNUN: Age identification at that time probably.

HATHAWAY: And what about the other areas, let's say theoretical physics? I'm thinking, you know, Delbruck read Schrodinger and that was his-- He was another physicist, but that was his raison d'être to go into biology. It was an obsession. His whole life was just making something from what Schrodinger-- Just theoretical and not based on any kind of-- You know, make it true with a kind of experiment. So that's what I'm sort of fishing for, I guess, is some sense that you see--Well, something I mentioned, a genealogy, if you will, of your experience, how you approach things. But perhaps, as you say, it was more general or generic. It was all these things together.

HANNUN: Yeah. It was all these things together, and I enjoyed it. I mean, the bottom line was I really enjoyed it. It was not very systematic. I would just—

There was a systematic component. Now that you remind me, there was. I did start with like the high school textbooks for physics and biology. I'm not sure about mathematics. Probably not. Physics and biology. And then I started going into undergraduate textbooks.

HATHAWAY: That's where I'm at. [laughter]

HANNUN: In physics and biology, when I was still in high school. Mathematics I kept more as a pure hobby. With physics, I know I tried to understand better quantum mechanics and relativity, but it got to be very frustrating towards the end because for that I needed sort of guidance. I needed to discuss things, and that wasn't available pretty much. With mathematics, it was much easier to just pick up anything and see how someone solved the problem, either from the history side or sort of a book side of things. Either way it was always gratifying. So the desire to go into mathematics, to go back to your question, waned with time, as the reality sort of took over and medicine became-- Medicine was always like--what's the right word to describe it--the fallback option. I mean, I knew my father was a good physician. He enjoyed it. I thought that was always a viable fallback.

HATHAWAY: And there was still all this stuff you were interested in, science and—

HANNUN: Yeah. I would explore science. As the interest-- My conviction that I could not make a rewarding-- I mean, I didn't want to become a college professor in mathematics. That wasn't my goal at all. just didn't have that aspiration.

HATHAWAY: And that's really-- I mean, if you want to become a mathematician, there's not much else. Either that or an actuary.

HANNUN: Yeah. I was interested in how creative I could be in mathematics. I know I was good in solving problems, but that's not the same thing. And I didn't have the opportunity to do that. So I think with time I went back to the sort of fallback, the concrete option of becoming a physician. But I think from that I started building the intellectual sort of direction to that, which is to get more into the biological science within that context, if you will.

HATHAWAY: This is, in a sense, even before any real definite choice has been made on your part that med school will be it or that "I will become a practicing physician," right? I mean, this was high school.

HANNUN: Yeah. Correct, high-school-level-decision sort of analysis. You know, the fallback position actually still is clinical practice, being a physician. It's funny. It's always been in my mind like the fallback position. When I was thinking whether I would go into mathematics or medicine, I would say, "Hey, I'm going to do the undergrad mathematics but at the same time fulfill the course requirements for medical school." So it was always the fallback position. It still is in terms of how I'm a researcher but also a physician. So that still is a fallback position. I must confess that I enjoy clinical medicine tremendously. I know many physician-scientists—

HATHAWAY: They want to back off from that. That's why they're the scientists.

HANNUN: Yeah. They're the scientists because they don't want to—

HATHAWAY: Have you much--? Maybe we're jumping ahead, but just at least so I know to approach it later in more detail. Are you doing much clinical practice here?

HANNUN: Not much. I do rounds on clinical services two months a year.

HATHAWAY: So do you just really drop everything here and go do that?

HANNUN: I can keep sort of the status quo in the lab, but I can't do much more than that during those two months. My function is more of a supervisor-consultant.

HATHAWAY: You mean here in the lab?

HANNUN: No, in the clinic. Teacher rather than primary caregiver. You know, I round with the house staff. I round with the fellows, but I don't see patients in my clinic, because otherwise that kind of commitment becomes too open-ended and I wouldn't be able to do my lab work.

HATHAWAY: And you can just sort of do it for two months and then walk away from the patients.

HANNUN: Yeah. Exactly. Especially with my specialty, you know. Where most of the patients have cancer, you just can't do it. If you want to treat those patients, at least our model here is you're very accessible. And if you want to keep that, you can't do lab work.

HATHAWAY: I think rather than go through any more kind of systematic year-by-year approach to your college education and things like that, we could perhaps--Actually, I want to go back and cover a few things but just kind of take up medical school as an experience and then the transition over into also some interest in basic research. But first, one, you said that as your parents loosened the reins on you guys because you did pretty well in school, you said that at some times perhaps as a teenager you weren't-- I'm not even sure I recall the word. But I get the impression that you thought perhaps your behavior was not that of the most upright young man but perhaps you got into trouble.

HANNUN: I didn't get much into trouble.

HATHAWAY: I'm thinking more of your social [life] and what a kid's life is like. Without asking directly for all the bad things you did, but more just your group of friends, or if you were perhaps much more of a loner, that sort of thing, just what it was like outside of the classroom and the library.

HANNUN: Let me put you in some sort of context there. First of all, there was a lot of free time growing up in terms of activities after school. I mean, society did not offer children anything

compared to what any normal kid would have in this country. There's a lot of free time after school, almost nothing structured to do.

HATHAWAY: No sports teams or high school bands or debate.

HANNUN: No. Very little of that. Even television would start later in the evening. It wasn't all-day television. Boring television, too. Summer was long and idle, very idle. Summer was probably a good three and a half months' vacation time. So there was plenty of time to do many things. It wasn't like I was either at school or in the library or reading at home. I mean, there was really plenty of time. And the other thing is mobility. From that part of Ras Beirut you could get from anywhere to anywhere else within ten to fifteen minutes walking. So it gives you a lot of mobility that way. You don't even have to borrow your parent's car or anything. I was a very outgoing person. I had a big group of friends, I would say. To the contrary, growing up as an adolescent, as a teenager, my behavior wasn't really bad, except I had very long, ugly hair. I looked very uncouth, just a rebel-type teenager. I look at my pictures now. I say now, "How the hell did my parents accept that?" I think I wouldn't accept that from my children. How did they accept that? That's why I put it in that context, that they were pro education to the extent of that's even okay. You know, "He's doing so well at school, that's okay. He can look whatever he wants to look like." I actually had a lot of extracurricular activities. I was very heavily into swimming, so very rigorous swimming training.

HATHAWAY: And that was organized, I mean, either in the community or in the school?

HANNUN: Both. Again, the school functions were very rudimentary, mostly in the community clubs.

HATHAWAY: So it's competitive-type swimming.

HANNUN: Competitive swimming. What else? Then hanging out with other kids.

HATHAWAY: Maybe smoking cigarettes or whatever it is. I'm thinking about again my own [youth] or American culture.

HANNUN: Yeah. I wasn't much of a smoker. I never liked it, but hanging out with people who smoked or whatever. And I really hung out. And again, something I wouldn't now understand, during school days I would maybe not come back home until midnight.

HATHAWAY: And this, again, is high school and not quite twelve or thirteen, more like fifteen, sixteen.

HANNUN: Maybe more like fifteen, sixteen.

HATHAWAY: And your parents weren't concerned.

HANNUN: They weren't concerned. I think the barometer was "How well is he doing at school?" And in retrospect I think I must have-- I mean the trust must have influenced me indirectly. I didn't need prodding to act responsibly, maybe because they were so trusting.

HATHAWAY: And they treated your brother and sister in sort of the same way.

HANNUN: Yeah. Same way. In many aspects, I was sort of the one to initiate things, and then my brother and sister would have that option. I like even competitive swimming. I started that at maybe ten or eleven, and my parents were hesitant about that. But once I got into that, my brother and sister would—

HATHAWAY: Because it would again cut into academics.

HANNUN: Yeah. Again, sort of hanging out with friends. I know my brother never had problems with that. Initially, I may have had some. I distinctly remember the summers being long and boring, even with having two hours of swim practice every day, reading a book maybe every couple of days, and hanging out with friends for another few hours. It was still long and—

HATHAWAY: Your family didn't travel outside.

HANNUN: No. My family didn't do much traveling. My father was a hardworking physician. I mean, he would work twelve hours. Or at least he'd leave at seven, come back at seven daily, and he wouldn't take off. I don't recall him taking a vacation ever.

HATHAWAY: And as things got more tense in Beirut and Lebanon in general, was the--? I mean, you talk about this area, you know, almost this oasis among all the different struggles and conflicts. Was it really pretty much an area that you knew you were restricted to? In other

words, you didn't walk into the Druze neighborhoods or the Maronite?

HANNUN: Yeah. As things became uglier, we were pretty much confined to that area. And it got uglier with time. Now and then it would improve a little bit but then get back even uglier. But at that time I was in medical school.

HATHAWAY: You weren't about to go anywhere.

HANNUN: I spent medical school hours in hospitals, basically.

HATHAWAY: Twenty-four hours.

HANNUN: Yeah. Pretty much that. Actually, one aside here is sort of my name didn't help matters either. For some reason my name, Yusuf Hannun, by Lebanese standards, would sound like a Maronite's name.

HATHAWAY: The last? We're talking about the family name?

HANNUN: The first name Yusuf in Lebanon is much more frequently used by Christians.

HATHAWAY: Because of the perhaps—

HANNUN: For some reason. It's a very common name. It's a very archaic name, a very old name. It's Jewish, European. All cultures have a Yusuf or a Joseph or something. But in Lebanon for some reason, unlike in Jordan, let's say, or other countries, it was much more associated with Christian names. And the last name was very ambiguous. There were Christian and Muslim families in Lebanon with that name, so that made it particularly hazardous. I mean, I could be nailed by any group basically. I wouldn't be comfortable.

HATHAWAY: I guess that's where maybe we should end up today. You mentioned earlier on tape that the realization-- Again, there was really more of a subconscious thing or something that you were always prepared for. That staying in Beirut wasn't really going to be an option at some point or that things were going to get worse and worse. And you're also at an age-- Admittedly, your concentration was on your studies as an undergrad, I'm sure, but in med school, and then in residency or whatever, much more intensely that way. But as you said, you

could get nailed by-- Politics and all these issues were constantly surrounding you. I'm wondering about your political involvement or about how-- Were you almost forced to and you refused? I'm trying to get a sense of how one dealt with what must have been daily kind of encounters with movements and sects of movements and just sort of your commitment.

HANNUN: Politics is a very strong element, or was, in Lebanese society. It absorbs a lot of people's energy. I attribute it, in my simplistic analysis, to the fact that people don't work as hard. They're not as much trying to achieve, and therefore they don't spend much time doing their work. I mentioned that's the trade-off, whether you want to keep the roots and then say, "Okay, what job can we find you so that you stay here?" And then you get a job, and you're not particularly excited about the job, and the job doesn't really depend on you either. I mean, government functionaries in Lebanon would probably work three hours a day at best and then spend the rest of the day bullshitting around or going to another more real job. So there's a lot of this idle time.

And people don't engage in a lot of either hobbies or productive activities. They engage a lot in just cafe-type discussions, and that's on a daily basis. People would also engage in all kinds of social activities the whole week round. It's not like, "Oh, we'll go out Saturday." People go visit each other during the days, during weekends. So it's that kind of atmosphere.

HATHAWAY: And you're ascribing that to the situation and the tension in Beirut, to the cultures that are there? Or just all for every human culture?

HANNUN: Not every-- That was Lebanese, maybe Middle Eastern. I mean, I have my own unsubstantiated analysis.

HATHAWAY: Well, that's part of what we do when we interview is to try to get these opinions, which are as important as facts.

HANNUN: I think the economic basis of wealth in the Middle East has made it very easy for people. With the oil, in the oil-rich countries-- Definitely the people in the oil-rich countries never sweated it out. And they're given handouts, hundreds of thousands of dollars' worth of handouts, and that's why everybody's happy and there's no discontent there. But it's also filtered down a lot to the Syrian, Lebanese, Jordanian, and Palestinian communities because a lot of those people went and worked in the [Persian] Gulf, including my father. But most of the people who stayed in the sixties, unlike my father, made a lot of money, because the sixties were the boom days of the gulf. And those were the days when that part of the Middle East--Syria, Lebanon, Jordan--were the interface with the rest of the world for the gulf region. A lot of people made megabucks there at that time and were supporting their family. It was easy basically. I mean, you could be a millionaire without having sweated it much. And that

permeated society to a great extent. It didn't get all the way to the lower socioeconomic strata. It didn't filter that much there. That stratum was, I think, the root of all the strife in Lebanon because it was totally underprivileged and uncared for. But a lot of the sort of more professionals that you would equate with the hardworking class, let's say, in the States, were not hardworking people. Many were. would say a few were, but most were not. I know my father was a very hard worker; other people that were acquaintances worked hard. But many were not. Many would have just all kinds of idle time. By and large, a lot of the people-- A government employee or even bank employees-- You know, the banks would close at one o'clock.

So this idle time I think fermented a lot of this or allowed the fermentation of a lot of this political discussion, not that it was any more intelligent than what conversation you could have with someone else about U.S. politics where you only discuss it once every two weeks, but they were engaging in it day in, day out. And with the civil war, there was a lot of pressure, first, to understand what was going on, because your life could depend on it if you go in the wrong neighborhood. You don't want to do that. And it took a few years before things really got defined, demarcated, at the geographical level, because when the civil war first started I didn't know that this area was mostly Druze and this was mostly Maronite. But obviously within two or three years that became very evident.

And the other thing is, as things polarize what happens is-- That's a general statement too. I always like to make sure those are clear. As a scientist, I hate to make general statements. As things become polarized and friction arises, what happens is those different sectors of society relinquish decision making to the wrong people, just like what's happening now in Bosnia. It's not the moderates who are running the decision making. The Serbs have relinquished their decision making to the militia leaders. And the Bosnian Muslims the same and the Croats. The same thing happened in Lebanon.

HATHAWAY: They had more than just this nationalist interest at heart--their careers and whatnot.

HANNUN: You give decision making to these people who are either criminals or with very strong criminal tendencies who are willing to go and murder for you. You first accept that "Hey, they're going to protect me."

[END OF TAPE 1, SIDE 2]

HATHAWAY: I'm going to try to remember where we were. I think you were discussing a situation where the tensions were growing and the pressure was on. But you'd also gone by way of talking about how the people were giving the opportunities to the wrong people to answer these questions or solve the problem.

HANNUN: And suddenly, or not very suddenly, the society in Lebanon was run pretty much by those warlords. So that set the forces backwards. And then the pressure was on everybody to basically, willingly or not, belong to one group or the other. Definitely for Lebanese it was so much so. If you were a Maronite and you didn't support your Maronite warlord, you'd be in trouble, and definitely for the Druze and whatever the same thing. I think people in Ras Beirut were still much more protected from those, just because of, again, daily interactions with other people of different backgrounds.

My personal involvement is-- I mean, I was always interested in Palestinian nationalism and sort of always felt the injustice to the Palestinian people, especially the people in the refugee camps. I always considered myself lucky in having a lot of options. But obviously the people in the camps were victims of almost everybody. That obviously panned out in time in terms of how they got beaten by the Israelis, by the Lebanese Christians, by the Lebanese Muslims, by the Syrians. I mean, everybody who said they were their enemy beat up on them. Everybody who said they were their friend beat up on them.

HATHAWAY: And the massacre—

HANNUN: And the massacre, yeah.

HATHAWAY: That absolutely nobody had their interest at heart.

HANNUN: Yeah. So I always felt those were sort of helpless victims. That was sort of my sense of civic responsibility. I think I'll put it more as civic responsibility rather than political responsibility.

HATHAWAY: Do you find the same criticisms you have for, let's say, the different Lebanese groups, which obviously have outside, clearly outside influences, as well, and actually rely on them--the Syrian, the Iranians, in the case of the Maronite--? God knows it's a different group of the Israelis at one point, right? Everyone's using this as-- Again, the people who are supposedly representing certain Lebanese groups are using it for the furtherance of their own power, but also the foreign or outside are using it for their influence within a situation. Do you see that there's something like the PLO [Palestine Liberation Organization] as also kind of outside-inside or do you see that as having some sort of more civic, let's say, and less political approach to--?

HANNUN: Both. Definitely the PLO was as much shattered by outside influence as anything else. The way I look at the Lebanese conflict, again, just to sort of put things In context, is that there are many tiers to this conflict. There's the age-old conflict between Lebanese Druze and

Lebanese Maronites who lived in the mountains. Then there's the more general Lebanese conflict between the different sects and the Shiites trying to aspire mostly for a bigger share of government, since they were mostly cut out of that. And then the Maronites and to a lesser extent the Sunnis trying to prevent that. But then the regional conflict, you know, Syria and Israel playing their own war games and tug of war, basically, through the Lebanese factions, definitely feeding that conflict a lot. And then, obviously, the more global conflict was between the Soviet Union and the U.S., sort of polarizing that even further.

I think that global context was a necessity for the regional context, which was a necessity for the Lebanese conflict. I mean, it wouldn't have been possible for Syria and Israel to play those games if they were not selling themselves as subserving the interests of the U.S. and U.S.S.R. respectively. And definitely the Lebanese people wouldn't have been as well armed and financed if they didn't get money from Saudi Arabia and Syria and Israel and Egypt. I think everybody around there gave arms and supplies. And Iraq and Iran. The whole region was engaged.

It was a pitiful game because the language of that political game was naked violence. That was the language, literally, meaning that you could send a message by blowing up a car. That was the level of communication. I mean, it's not hyperbole. It was blowing up a car in the middle of the market just to tell the leader of whoever controls that region, "Hey, we got to you today because you weren't toeing the line yesterday."

HATHAWAY: The same that's in perhaps Northern Ireland between the British and the IRA [Irish Republican Army].

HANNUN: Yeah. Although there the messages are much more clear-cut, that, you know, "Hey, we hate your guts, you hate our guts, and we're going to blow you up until you do--" There, I mean, it was even, what, instead of sort of France sending a message to Germany, "We don't like your interest rates," [Syrian President] Hafiz [al-]Assad could send a message to the Maronites one day or the other people the other day, "We didn't like what you said yesterday," and blow up a car. It was that level. The worst part about it is the people. We could never interpret those messages. We would see it as random violence, but we knew it wasn't random. Someone had planted that car bomb for a reason. You knew that whoever received that message knew exactly what the message was. It was a very sick game being played with human lives. Just to jump back to later years, when I was a resident in the hospital, you'd get a bomb--either an Israeli attack or a Syrian bomb or whoever planted a bomb somewhere--and you'd get two hundred casualties in half an hour. I mean, it was horrible. It was really horrible. So the pressure was there to—

So the PLO was both-- The other side, going back to your question, the PLO was obviously rampant with all these levels of conflict, one faction going for the U.S.S.R., the other aligning with the Saudis, so that they can align with the West and all kinds of things. But it did represent, and I think it still does, although I'm not much now in the situation, in the middle of it-

-Definitely, when I was in Beirut, the PLO did represent the sort of national aspiration of the Palestinian people. It did command their civic duties, meaning that if you were a Palestinian engineer and you wanted to do something about Palestinian refugee camps, you would go through that [the PLO] and do it. So it did command not only the political and nationalistic but also the civic—

HATHAWAY: And that's again where we started going, came from on this, was your talking about your direct sort of—

HANNUN: Yeah. So I mean, obviously, at the personal level, I would engage in whatever political discussions are going on, trying to probe why we think one way or the other. Almost invariably those were fruitless discussions. Towards the end, I got very disenchanted with the whole system. The whole social structure basically became very disappointing that would allow this kind of nonsense going on and on. Beyond that, in terms of political activism, I was on and off involved in-- I don't know how to describe it. Nothing significant basically. But I would always-- You know, if there are ways to help-- Let me give you examples. During '79, when Israel attacked southern Lebanon and there was a major displacement of Shiites and some Palestinians, I was very engaged in collecting blankets and food and whatnot.

HATHAWAY: You were either just graduating from your undergrad or you were just going into medical school, right, if you finished in '83.

HANNUN: I was early in medical—

HATHAWAY: Right, because '83 was actually when you finished your residency.

HANNUN: Right. So I was in medical school. It must have been '78, I forget the year, '78 or '79, when the invasion of southern Lebanon occurred. That was one time I remember vividly because we stayed engaged for many weeks on end. We set up a clinic to cater to those people. That would be the most sort of vigorous memory of that.

HATHAWAY: And again, we really are talking about--again, I think your distinction is much better than anything I could have come up with--the civic versus really the political, whereas that doesn't mean it [doesn't have] political ramifications. But it was, again, Shiites as well as Palestinians, and that wasn't an issue for you. It wasn't simply "Okay, which of you are Palestinian? I'll help you."

HANNUN: Yeah. I was very disenchanted with the political structure even of the PLO. I mean, even if I wanted to express my political nationalistic activism, which I did-- I would have liked to see the Palestinians improve their human condition. But the PLO was not the structure for me to express that, because I could just see it like another mess of things where you couldn't develop a healthy infrastructure. And I did have some encounters with people from the PLO or other militias. You know, immediately the first thing that comes across is that you don't want to be dealing with those people. You could get tricked into doing that, I think, if you develop sufficient hatred, let's say, against another sect, say, "Hey, I want to do to them what they did to us." I guess once you start playing the game of us and them you could get easily involved in that kind of-- But if you're thinking more long-term--how can you make the whole Middle East more peaceful and healthier and a productive area of the world--the minute you'd see those people, whether they're nominally on your side or not, you'd say, "Those are not the people I really want to interact with." They were not selected because they were popularly elected. They were not selected because they were doers in terms of doing good to the population, or achievers. They were selected because they could do the dirty work. That's not the way to solve the problem. I guess that was pretty much the extent of my political activity.

[END OF TAPE 2, SIDE 1]

[END OF INTERVIEW]

INTERVIEWEE: **Yusuf A. Hannun**

INTERVIEWER: **Neil D. Hathaway**

LOCATION: **Home of Yusuf A. Hannun**
Chapel Hill, North Carolina

DATE: **30 March 1993**

HATHAWAY: We talked a little bit before we turned this on. I think we pretty much decided we'll just kind of pick up where we left off and worry about maybe talking about some more general things toward the end where maybe there's a relationship there. Really where we left off was your going to medical school. I think we covered why and the impetus for going. I guess the only question or the way I'd start it off is to ask, was the American University [of Beirut] your only choice, or your first choice? What were the reasons for going there, as opposed to like your dad [Awni Hannun], I guess? I think he went to Europe.

HANNUN: Well, going to undergraduate at the American University was sort of a very logical progression at the time. And again, I guess from the cultural point of view, which is quite different from the U.S. culture, the family stays closely knit much longer than the U.S. family. The age of separation is usually not at eighteen. It usually actually comes after college rather than before college, and it's never as clear-cut a separation. The fabric is much tighter and extends into the extended family, not just the nuclear family. So going to the American University was a very logical choice. It was the usual norm there. At that time--and I have to remember here a few things--I did toy with the idea of coming to the States for undergrad. We talked about that a little bit. I really didn't feel like it was important. Maybe in retrospect I would have done it, I don't know. Again, I think the frame of mind of myself and most other people my age is you didn't have to leave home or your town when you hit eighteen and just go on your own. So staying there was a very logical solution. The other thing is I think the civil war was starting to brew. That must have been a little later on.

HATHAWAY: Yeah. I wanted to get it down for the record that you started medical [school] in '70—

HANNUN: In '76.

HATHAWAY: Okay. I wanted to say '78, but okay.

HANNUN: In ‘76. And the civil war in Lebanon started in ‘75. At that time, I sort of got trapped in staying in medical school at Beirut. The way the civil war started, it wasn’t clear whether it was going to escalate and become what it turned out to be or it was going to be a wrinkle that was going to go away. I guess people tended to stay together in sort of a more cautious approach to things.

HATHAWAY: I think in talking about the same period of time in our first session, maybe it was-- I think I’m thinking high school, college. Maybe I’m going back too far. You mentioned a sense of it just getting worse and worse, though. I guess I get the impression what you were talking about was-- And it wasn’t just you sitting there thinking about this all by yourself. Just a sense of all of you having to get out at some point. I mean, that there was just nothing definite, that there was certainly always in just the back of your mind—

HANNUN: In terms of--?

HATHAWAY: I don’t want to say impending doom.

HANNUN: More anxiety, maybe, at the social, societal level, anxiety. You could see the process fermenting, brewing, in terms of people becoming more polarized in their thoughts, more anxious, more exclusive of other groups. And that was prior to the onset of the civil war. With the civil war, sort of it started forcing people to take sides, even if they didn’t want to.

HATHAWAY: I guess I’m trying to get a sense of how much that might have affected your decisions about staying with your family, being near. Perhaps you even had conversations with your father or siblings about what the family was going to do. Maybe there were preparations starting to be made, because certainly everybody had had the experience prior to that of having to just up and—

HANNUN: I haven’t thought much about that, but I think there was a sense of maybe I wanted to be more practical at that point and really follow more a clinical career and stick with medical school and try to be more down-to-earth, more relevant that way.

HATHAWAY: And close to home.

HANNUN: And close to home. I don’t know. Remember, for us growing up in Beirut, the American University was really a highlight of education.

HATHAWAY: Obviously, it wasn't just a perception that was shared by people in Beirut of certain backgrounds, but also that's the perception of many people in the Middle East and the world. I'm talking about pictures in your yearbook of lecturers or visitors like LBJ [Lyndon B. Johnson] in '62 and [Jawaharlal] Nehru. Obviously it was an intellectual center.

HANNUN: It was. It was a highlight in the Middle East. A lot of the leaders in the Arab countries graduated from the American University of Beirut. It's probably like having Harvard [University] in the U.S. but not having anything else either. It's that kind of situation.

HATHAWAY: Cambridge [University] and Oxford [University] rolled up into one.

HANNUN: Yeah, and with very little in terms of other choices. I think after the civil war other options opened to people in the Middle East in general in terms of sending their kids to Europe or the U.S. But before that if you lived in Saudi Arabia, people would send their kids if they had the ability to. They would send them to the American University because it was an Arabic-speaking country and closer to home and offered really top education. The medical school in particular had an astounding reputation. [tape recorder off] The medical school was maybe in a way elitist, but it was the highlight of education in the Middle East by far, undisputed.

HATHAWAY: Was it really tough--?

HANNUN: It was extremely tough to get into. So again, in the good old days, probably even before my days, you were talking about selecting a class of fifty students from mostly the whole Arab population, not just Lebanon. I mean, you really were selecting the top young graduates from the American University as well as other places for admission to the American University.

HATHAWAY: I hope I also haven't been giving the implication that I was saying, "Oh, why didn't you leave and go to a better school in Europe?"

HANNUN: Yeah. I understand that. I have to explain sort of my perception at that time. It's very different from a kid going to high school in Durham [North Carolina] saying, "Well, do I go to UNC [University of North Carolina] or do I go to the West Coast?" I mean, those were really not the options available at that time. For one thing, the American University was it in the Middle East for a medical education. And the reputation was great because the medical school was primarily set up by solid academicians who came mostly from American medical schools and set up the different departments.

HATHAWAY: And they were American-born?

HANNUN: Yeah, mostly American-born.

HATHAWAY: So a mix perhaps, then, of Arabs and-

HANNUN: The faculty was-- You know, an Arab-Lebanese faculty was groomed, but it was really initiated mostly by American heads of departments. I think in the forties perhaps, 1940s and 1950s. I recall people saying [Allen 0.] Whipple of the Whipple procedure would spend a few months at the American University and so-and-so did. I mean, many of the big names we encountered in textbooks. Ray [Raymond D.] Adams, the top neurologist in this country—he's an older man now--was still visiting Beirut even during the civil war. The interactions were mostly, actually, with Harvard and with Johns Hopkins [University], a lot with Johns Hopkins. Probably the American University was the only sort of medical school outside the U.S. built on the Osler tradition.

HATHAWAY: I have some familiarity with that.

HANNUN: In terms of the apprenticeship system of William Osler, in having medical students have hands-on experience from the very beginning, in terms of the house staff training being not only hands-on but more like a boot camp, which it was until very recently in most medical schools around the U.S. As an intern, you just lived in the hospital. You just had no other life. Your life was the hospital, which was very important because, from my experience going through it and as an educator, it's the year where people undergo a transformation. So it was very unlike most European systems. Even in France and Western [Europe], it's more the professor and everyone flocking around the professor and watching what the professor [does]. It was a real hands-on experience.

The reputation of the medical school was great, so it was a very viable alternative to stay and go to medical school there. It was so well connected with mostly Hopkins and Harvard that most people who went through easily usually went on to have more specialty training at either Boston or Baltimore or go back or stay. So it wasn't like a dead-end situation. It was a very viable choice and, again, probably financially a much cheaper choice than going to the U.S. to a private medical school or something like that.

HATHAWAY: Do you mind my asking, is there any way you can equate what you were paying in tuition or something with anything that--? If you could remember how much it costs, say how much it costs.

HANNUN: It must have been around $3,000 for tuition. But remember, I was staying with my folks, so that was it for expenses.

HATHAWAY: Do you also know perhaps what the tradition or the attraction was for places like Hopkins and Harvard? You mentioned just offhand there was some administration being done by this board of trustees that was actually back in New York and not in Beirut, from World War II. I'm just wondering if you can—

HANNUN: I don't know the history of it.

HATHAWAY: Americans founded the place certainly.

HANNUN: I think it may have had to do as much with people at Hopkins or Harvard very interested in exploring international possibilities, and the American University stood out as sort of—

HATHAWAY: There was also a chance to get to a really nice beach in the Mediterranean! Who knows?

HANNUN: So I really don't know the historical background to it. I vividly recall, going myself through the medical school, that most of the faculty were Lebanese or Arab, had trained at usually either Hopkins or Harvard, mostly specialty training. There was definitely this kind of connection.

HATHAWAY: And is that where your opportunity to come to Duke [University Medical Center]--? I mean, we're just jumping ahead. We won't get into it. It was a tradition. It was a thing that many people did.

HANNUN: Yeah. The tradition was-- I think as the place was growing, up until the civil war, the American University had set up first-rate residency programs, which are sort of the initial specialty training, whether it's in surgery or internal medicine or what have you. Those were very powerful programs, again, extremely competitive. But they had not set up any significant subspecialty programs. So that was the end of the road with the American University. Most people who wanted any further training, subspecialty training, had to get it somewhere else, usually in the States, sometimes in Europe.

HATHAWAY: And so actually your father going to a place like Glasgow is actually more kind of against the grain or something. Or maybe there was no tradition, he just simply went because he wanted to go to med school.

HANNUN: When he started out, that was in the late 74.twenties.

HATHAWAY: Of course the British presence was so-

HANNUN: The British presence in Palestine was it. mean, they were it there. He did try to go to the American University. It wasn't yet sort of a premier medical school at that time. He did try to go there, but I don't recall the details. There were some funny incidents. He said, "I don't want to go there." And he decided to—

HATHAWAY: It still could have well been tough to get in just because there were many families or connections or something.

HANNUN: I think it was even more trivial than that. I think he wanted to play soccer and they wouldn't let him. It was something like that. It was real trivial at the time.

HATHAWAY: You were a mathematics major, right, as a undergrad, but of course, as you said, did double time doing all the requirements for the math major but also making sure you got all the requirements in for premed and being able to apply to med school. I don't know that you talked much about what that was like. You were obviously more interested in the mathematics, I think.

HANNUN: Actually, for a while I was more than a mathematics major. Let me recall that. Because when I went-- How did it happen? My first semester, my faculty adviser would not let me register for more mathematics courses, for as many as I wanted. I actually-- And this is another university. That was the Lebanese University. I went as a math major there. But after the first semester, my adviser let me take as many courses as I wanted. So that's when I sort of majored primarily in mathematics.

HATHAWAY: So the other courses-- I mean, you were taking just kind of the gamut of chemistry, organic chem, biochem.

HANNUN: Well, it was a rigorous curriculum. And for people who went into straight premed, which I did, it was a full curriculum.

HATHAWAY: Much like it is here, I take it.

HANNUN: No. Not even-- I mean even more so. I mean less flexible than the premed curriculum here. People had to take a fixed number of biology, chemistry, physics, English, and literature. I think all the course requirements amounted to very few electives, very few electives.

HATHAWAY: Right. Or as long as you took the three English classes from each century, you got to pick which class you took or which professor you ended up with, that sort of thing.

HANNUN: Yeah. Pretty much.

HATHAWAY: I'm trying to get a sense of what the quality--Again, you're mainly looking at biology classes.

HANNUN: As an undergraduate.

HATHAWAY: Or just as prep[aration] for med school, and then we can talk more about the med school classes. I don't want to make this a major—

HANNUN: Remember, I started at the university in '74, undergrad[uate]. There's a quirk there to the system, because we graduate from high school and the freshman year is incorporated in high school.

HATHAWAY: So it's three years you did--

HANNUN: Yeah. It's a whole combination of one being incorporated into the other. There was an option for non-Lebanese like myself to enter the university at the freshman level, but most people entered at the sophomore. So I entered at the sophomore level. I did the equivalent of a [college] freshman in high school. The same thing with medical school. There was an option for most people who would qualify to enter medical school in the senior year, and the first year of medical school would double up as the senior year. So that's why the premed curriculum was

pretty tight, because you could take it over two years.

HATHAWAY: And actually kind of one year was in high school. I mean, you're really talking about—

HANNUN: In addition to the high school year, you could take it over the sophomore and junior and then go into medical school.

HATHAWAY: Med school with a year under your belt.

HANNUN: Quite a number of people condensed it, went through the two-year program, but the same requirements.

HATHAWAY: That's what you did.

HANNUN: That's what I did.

HATHAWAY: I was going to say, you entered in '74 and you've talked about med school beginning in '76.

HANNUN: So it's a little confusing because sort of the freshman year you do in high school and the senior year you do in medical school. It was really only two years of your usual undergrad. The quality of education was excellent from the didactic point of view, excellent. We talked about that the other day a little bit also. In terms of the creative aspect of it, I think as compared to my high school experience, if anything, the didactic part was not as superb as the high school experience, but the creative aspect became more available.

HATHAWAY: What examples might, you know--?

HANNUN: It's very haphazard, very much dependent on the teacher and the course, rather than on a program or a department. Let me think. My theoretical physics was wonderful. I had a very brilliant teacher who just engaged us in all kinds of ad-libbing theoretical physics rather than follow a textbook. Our botany teacher, the second or third week into the course, turned against us pretty much. I guess the class started becoming rowdy or something, and he just became the most horrible, didactic teacher. There were some literature courses that were wonderful, English

courses horrible.

HATHAWAY: When you say literature, then, you're not talking about just literature taught in English or-

HANNUN: There were required courses in English as a language.

HATHAWAY: Like composition and grammar.

HANNUN: Yes. Yes. That kind of stuff. Those were horrible. Arabic classes, the ones I took, were very uninspiring, I think.

HATHAWAY: And those were literature, more literature study, reading.

HANNUN: Yes. Reading and some writing too. Mathematics, again, some were wonderful and brilliant, and others were not. Organic chemistry was good, but I didn't like it at that time. Actually, while I was doing my mathematics, I somewhat resented the premedical curriculum.

HATHAWAY: And you were really more geared-- I guess I'm also trying to get a sense of what your perceptions were. As you said, you'd become more practical, given the situation you found yourself and your family in. But you also had this lifetime's experience of what it was like to be a doctor, I assume, with your father, I mean, whether he took you on rounds every day or not. You still had to have some sense of what a doctor does, how a doctor does it, and that sort of thing. And then here you are having to take these prep classes.

I'm also, on top of all that, trying to get a sense of your own feeling-- Are you just going into something to do? You know, in 1974, '75, '76, biology, like it had in the early 1950s, had just come full circle. It was taking off. And I was wondering-- I've noticed there's a wide variety of responses, because you [Pew scholars] all basically were undergraduates or just thinking about continuing a career in biology or health or something when this happened. People have a wide variety of experience with it. For instance, no such thing as molecular biology was being taught to undergrads at all until '82 or something like that. So I'm also trying to get just a sense beyond your reaction to it of what was being-- Did you have an idea of what biology and medicine were, in a larger sense, beyond your father's practice?

HANNUN: No, not really, actually. Not really. And even my father was very remote from my decision making. If anything, at the intellectual level, I did not like my father's model of clinical

practice.

HATHAWAY: Because it seemed boring?

HANNUN: His was really down-to-earth taking care of patients, day in, day out, a very hardworking person.

HATHAWAY: Not a specialty and not sitting in an office. He was out—

HANNUN: He was an internist. He was working very hard, and he was motivated to take care of that group of patients. But you could see the price he was paying for taking this kind of career.

HATHAWAY: You mean emotionally.

HANNUN: Emotionally it was draining. Tough patients to deal with, mostly uneducated, poorly educated.

HATHAWAY: Maybe few results in the preventive area, right. You treat them, but they'd come back with the same—

HANNUN: All those kinds of frustrations. I always respect his dedication to that work. But in terms of a model for clinical medicine, if anything, I probably, in retrospect now, since you ask, didn't like that. I never thought of it that way before. I didn't want-- It was something that I was ambivalent about, I guess.

HATHAWAY: I was going to say, what other models maybe did you have? Maybe the American University.

HANNUN: At that time, probably, honestly, I didn't have too many role models.

HATHAWAY: This was a real practical—

HANNUN: Yeah. And going through undergrad, that was part of the resentment in going

through the premedical curriculum. On the other hand, I had decided that math was not going to be my long-term career. I wanted to enjoy it in undergrad, and I did that. But I also resented a lot of the premed. The premed mentality--Again, to put you in that perspective, there was a major selection among premed students for medical school. I don't recall the numbers any longer, but it could have been as many as three to four hundred students, entering premedical students, with only fifty being accepted at the end.

HATHAWAY: Fifty from American University plus others—

HANNUN: Plus a few others from other places. Mostly from their undergrad. It was extremely competitive.

HATHAWAY: It was happening right there in front of you, as well. You know, if you were all applying to Harvard, you live in a thousand different places. You live in the same town—

HANNUN: It transformed many people, and you could see it transform them. I didn't like that. I didn't have any difficulty in getting high grades, so I wasn't worried about myself. But I resented the fact that I had to be In this kind of rat race.

HATHAWAY: If I can interject for a second and, again, not to really go after something-- You talked about "resenting." That feeling-- I'm wondering, did you have a sense of what it was or who it was you were resenting? I mean, was it life in general, all of mankind, your parents? I'm just curious to get just a general—

HANNUN: No. It was a very focused resentment. I was happy being at home. I was totally free. It was like renting out basically. Very good terms with my parents, my siblings. Many friends. I always did things with friends, always had the time to do that. But intellectually the premedical program was uninspiring. And I sort of at that time-- To be very honest here, at that time it was like a gamble to me that there was something good about medical school, but I definitely did not see it in premed. That was a source of that kind of resentment. I think that, again in retrospect, was justified, because once I hit the clinical years in medical school I loved that, I loved that. But the premedical program, I didn't like it. It was a rat race. A lot of my friends just got sucked into it. I could see them struggling and many dropped out. It was a lot of pressure, sort of family pressure. "You either become an engineer or you become a doctor." In the Middle East, lawyer is not an option.

HATHAWAY: It's no longer being considered much of an option here either. Well, that's maybe not completely true yet. I was going to say, what were the other options? I mean, I guess

there weren't any. This isn't just an issue of peer group pressure.

HANNUN: Yes. Exactly. I mean, for me, if you ruled out theoretical physics or mathematics, engineering was the other option of sort of acquiring a professional career. Many people went into business if they had the family support. You know, if they were born into a wealthy family, they knew they had a business to grow into after they graduated. But other than that there were very few opportunities for professional education and professional careers. I think that's a true statement.

HATHAWAY: You also brought up--and maybe not directly, I mean not in this context--the sense of how you looked around you in Beirut and saw a lot of people who were idle. And I assume perhaps that was another option, right, especially if your family could support you or you could just hold some sort of a job that was even semiprofessional or not a job at all, especially in times when there was real doubt about what tomorrow would bring or this holding-pattern situation. You didn't talk with negative things to say about this, but you mentioned that you saw around you a lot of people who—

HANNUN: Were idle.

HATHAWAY: And then became almost kind of like, as you saw, perhaps a detriment to any solution to the problems that were facing both the Lebanese and Palestinian communities.

HANNUN: Let me see if I got your question. I think, for me, being idle was never an option. I mean, to put it that way. I think in retrospect I could explain many things by saying I was always looking for a career that would intellectually grab me full-time, twenty-four hours a day. In retrospect, it's easy now to understand those forces because at that time it was maybe more resentment or anxiety. But now I can easily see how I could never be a nine-to-five-job person. The vacuum that kind of job would leave in me would be just horrible. I could not be someone in a career basically that did not grow intellectually with time. So that eliminated a lot of options for me. I think in retrospect, again, I was always steering away from all those kinds of options.

HATHAWAY: And I guess I was kind of just mulling around or just kind of bouncing around this whole area, because, again, I get a sense that the situation you found yourself in, the compromise with the premed-- And, of course, you later came to realize it was not so much of a bad compromise-- But now, the time we're talking about, you haven't figured that out yet. It must have been stifling. There was this uncertainty. There were limited options. And here's somebody who said that it wasn't even an option to think about not-- I mean, just kind of hanging out for five years. I guess maybe I expect more anger. Not that you have to fit my view of things, but just you seem to be—

HANNUN: Yeah. It was stifling. I think that may be a very good description of my emotion, why my reaction was that way. But again, I don't think my reaction was-- I don't want to say it was anger. If I was growing up now in that environment I would be angry, because I know different now, I know what other options are. I know what good education is. I know what creativity is and how that can be fostered. But back then I really didn't know that. I felt like I was missing something. I was maybe being stifled, but I really didn't know what I was missing. So I don't think anger was a major-- There was some resentment, but not anger necessarily.

I would resent going to biology. I mean, biology class was at eight o'clock. I would never go to biology class. Small things like that. Organic chemistry, always made a point of going fifteen minutes late to the lecture, almost adolescent resentment of being part of that game. Again, in retrospect, I think it was that stifling component. I was in search of something that would fulfill me and have a long-term prospect. That's why I dropped math. I knew math would at that point provide a lot of fulfillment, and it did. It definitely did for those couple of years provide me with a lot of fulfillment.

Along those same forces, the first year of medical school was the pits because the first year of medical school was actually much more a continuation of premed than an entry into medicine. The courses were lousy basically. With the exception of neuroanatomy that we had and gross anatomy and some biochemistry, all the other courses could almost have been premed courses. And at that time I couldn't do my math. I couldn't do any other thing—

HATHAWAY: But med school, right, of course.

HANNUN: And that I resented. In the second year, things started turning around.

HATHAWAY: And this method you mentioned before, this mentorship or apprenticeship method kicked in the second year then.

HANNUN: It started a little bit in the second year, but then we started studying real medicine. We studied pharmacology, the body systems, physiology, microbiology, and interacting a lot with clinicians. So we were starting to interface with the clinical. I thought, "Hey, there's so much to learn there." I was really excited about the dimensions of this new knowledge.

One thing I have to bring in about all this, because parallel to what I was just describing about my own personal reaction to the educational system was the civil war. The civil war was brewing in '74, kicked in in '75 in ups and downs, and towards the end of my junior year all hell broke loose in Lebanon. I was actually on a vacation in London, England. It was probably the only vacation I took without my family outside Lebanon. I'm trying to double-check on that. I

got stuck in London because I couldn't get back. Now, come to think of it, that's when I also was about to register at Imperial College [of Science and Technology] for engineering.

HATHAWAY: Okay. This is a story I haven't got a sense--Because you were stuck you looked into it.

HANNUN: Because I was stuck. That was definitely because I was stuck.

HATHAWAY: Never stopped for a minute, right. You would just pick up and-- I mean, if you were going to be in London for, oh, a year or six months—

HANNUN: Yeah. I better do something about it. I corresponded with my father, and he said he could support me partly. I went to Imperial College, and they offered me admission and some support. For some reason, I had--Or maybe my father sent me my transcripts or something. So it was real easy, based on my transcripts, to convince them that I was a good candidate.

HATHAWAY: Prospect, right.

HANNUN: Yeah. Prospect.

HATHAWAY: Had you friends there? I mean, were you really kind of like stuck in the middle of London without family or friends?

HANNUN: We sort of were a group of three, I think, who traveled there, and we met with another group of a couple of other people. So we ended up being six, seven people who got stuck there. The airport was closed in Beirut. I thought, "If I'm stuck here, I'm going to make something useful out of my stay." I thought engineering would be a good option. Three or four years and you're done with it and you have a career and just get it going. Obviously,

HATHAWAY: supporting I couldn't see myself idle in London. Or with the prospect of not having any way of yourself, being, I guess we use the phrase, "down and out."

HANNUN: I did have a friend there in London who had already sort of bailed out from Lebanon and went to London for education. That year, '75, many people started bailing out. Many of my friends started bailing out, and that continued throughout the years. Because now if

you ask me who of my couple of hundred friends that I had growing up remains in Beirut, probably there are only two or three.

HATHAWAY: And why didn't you go? Had you considered--? I mean, it didn't take you long to think about doing it for practical reasons as well when you were unable to get back to Beirut. But had you thought, "Oh, I'll just kind of pick up medical school somewhere else, and I'll get the hell out of here."

HANNUN: I think I tried to look into medical school, but it was pretty difficult in England to get into medical school on that short a notice. You know, basically it was I think late September or something, walking in, saying, "Hey, I'm stuck here. What's available?" Medical school was not available.

HATHAWAY: But you hadn't thought about this while you were still in Beirut. As you say, your friends started leaving in droves.

HANNUN: In terms of bailing out, I'm sure it's something that had come up dozens of times with my friends.

HATHAWAY: I meant more seriously, like you'd sent off that application and got that plane ticket.

HANNUN: It never became serious.

HATHAWAY: Sat down with your father to figure out the logistics of doing something like this.

HANNUN: No. It never became serious except when I got stuck. But then things quieted down, the airport opened, the medical school opened. I went back. So there is this sort of parallel going on with the civil war there that I'm sure affected a lot--maybe not a lot--but did affect my decision making.

HATHAWAY: It would have had to if the whole community that you expressed as being very close and something you actually kind of miss in American culture and here in Durham--Although I guess we're not in Durham right now, Chapel Hill, but, you know, in this area and in this part of the world. It must have had some effect, again, not anything direct that we can

calculate.

HANNUN: I don't think it's something very direct to articulate.

HATHAWAY: It must have been frustrating. I mean, you had a goal in mind--finishing med school. But did you have beyond that? Some people really, really plan their lives.

HANNUN: I didn't really plan my life. One of the ironic things is-- Again, in medical school there were many excellent role models, people who were either good basic scientists, very few-- There were very few basic scientists, but they were very good role models. And there were many very good role models for clinical medicine, very thoughtful, well-read, perceptive people, analytical. The system there-- I mean, its excellence was derived primarily from those kinds of people, because clinical research or basic research was not the forte. It was the education.

HATHAWAY: I guess that's what I wanted to go to. You know, it was the hands-on stuff and the experience with--I'm sure we can even name names if there are two or three particular mentors you have in mind or people you came in contact with as a med student. I wanted to know what that spark was that kicked in and made you decide this wasn't-- And I think actually, yeah, why don't we do that? I asked the question on this side, but you can answer it on the other.

[END OF TAPE 3, SIDE 1]

HANNUN: So you're done with your question, I guess.

HATHAWAY: Unless you had more to add about the experience of being kind of stuck outside.

HANNUN: No. That was really transient, and it's never something I hesitated to drop once I had the option to go back and finish medical school. So it wasn't really—

HATHAWAY: And this is far enough along in the process that you already had that spark.

HANNUN: What spark?

HATHAWAY: You said something about how in the second year it finally-- I think you used the phrase "kicked in."

HANNUN: There were a couple of things that happened in medical school that I did not anticipate when I was a premed or even before. One is the enjoyment of clinical medicine and the satisfaction that that gave me. I knew that that would be a good career, but until I had sort of the second year and definitely the third year of medical [school]--which is where the clinical stuff really kicked in--I really did not have a good anticipation of that. Had I had that anticipation, probably things would have been more palatable to me in terms of premed and what have you. So that was--I don't want to call it a spark, not even a revelation--a very positive thing that happened. It was intellectually very stimulating. There was so much to learn about the human body in health and disease. The hands-on experience in clinical medicine was very gratifying because you could easily be called a doctor even as a third-year medical student and would deal with patients as their primary caregiver under very close supervision and whatnot. And again, the role models there were very good, were excellent clinicians that mostly were very stimulating people.

Now, the other thing that was starting to develop at that time was sort of the interest in biomedical research. That's sort of a very funny story there. There's a twist to it, because when I was even in high school I considered sort of shortcutting all that and going into-- As one option, you know, considering many options, considering going into biomedical research, either some biochemistry or microbiology or something like that, one of the biomedical research areas. In high school, there were many people who were invited as role models to discuss career possibilities and whatnot. The person [Ibrahim ^{p}urr] who came to discuss with us biochemistry and microbiology sort of made me think, "Hey, I don't want to do that." It's very ironic because that person turned out to be my biochemistry teacher who I came to like very much and respect a lot. I don't think I ever told him that.

HATHAWAY: A biochemistry teacher in college.

HANNUN: In medical school.

HATHAWAY: Okay. So he came down from the university.

HANNUN: When I was still in high school. I said, "I don't want to consider that." It was sort of a generic conclusion on my part that I still think was significant, that I didn't want to pursue academics or a career in research at that time and sort of left it at that. And then the research option started growing again in medical school. I don't know if there was a spark there that sort of got me into biomedical research or if it was more a gradual process. I think it was more a gradual process. I enjoyed biochemistry a lot in the first year. That was pretty much the only

course I enjoyed. I enjoyed understanding, or the goal of trying to understand, how the body works at the level of the molecules and reactions, biochemical reactions. I thought that was fascinating. Again, one is influenced by role models perhaps.

A couple of biochemists there were very smart people, a very positive influence on me. We also had a person [Naji Sahyoun] come in. He was several years our senior. He had finished his M.D. That's a long story that also intersects my career choices a couple of times at least, or actually more than that. He had come to the States to-- Actually, he did not follow the normal track by Beirut standards of going through residency and whatnot. But once he finished medical school, he came to Hopkins to do biochemistry research.

HATHAWAY: So in a real sense he was kind of a model. I mean, even though you didn't do it his way, you knew that was—

HANNUN: Yeah. What happened is my first year of medical school was his first year of coming back to Beirut. After doing a lot of training--several years of training, or maybe two or three years of training--he went back to Beirut and taught part of biochemistry. He sparked a lot of interest in many of us in sort of research.

HATHAWAY: Was he doing some there?

HANNUN: He did some in Beirut. He did some research in Beirut.

HATHAWAY: Kind of continuing what he was doing.

HANNUN: I think so. Some of us started poking our nose in and just finding out what was going on. And again, in the setting of the American University, by that time it had become unusual. Apparently there was a strong tradition of research in the medical center in even the thirties and forties and fifties.

HATHAWAY: Clinical, I mean, kind of applied--

HANNUN: That and very basic research.

HATHAWAY: Oh, so basic, not really related at all to treatment.

HANNUN: I think with the civil war that was the first thing to go. I mean, from day one of the civil war that was eliminated.

HATHAWAY: Was the government funding some of that? This was all private-endowment type? I mean, I'm just curious. Obviously, it seems above the fray of politics for almost forever. And it was only the outside forces that kind of brought it directly into political-

HANNUN: I don't know what were the major sources of funding. I would say most of it was university funds and maybe some government funds. But that was really the first to go, because by the time we hit medical school, which was really the first year of the civil war, it had gone. It had come almost to a screeching halt. So that was really something different at that time, finding someone setting up some experiments and things like that. That was a very strong influence at that point.

HATHAWAY: You were taking biochem classes even as an undergrad. Obviously microbiology and all the curriculum was there. But there was, in a sense, then, no-- I mean, a common-- Not by any means the majority, but a common avenue into discovery about research and, "Oh, wow, this is fun," is undergrads who all of a sudden are summer interns in what turns out to be similarly interesting.

HANNUN: No. The opportunities were not there, and that's a recurrent theme. Biochemistry was a first-year medicine course. It wasn't undergrad. Undergrad, the kind of labs we took were so anticreative that—

HATHAWAY: And they were just to repeat the same thing. "All of you do twenty of--"

HANNUN: You wouldn't believe it, but biology probably still involved dissecting starfish and whatnot. It was very primitive biology lab work. Chemistry, inorganic chemistry, was also very primitive. I don't think even organic chemistry had the lab. They probably didn't offer a lab for the premeds. There was this sort of herd mentality that premeds are there for the grades, they're not there for-- It was sort of a mutually reinforcing situation, where the premed students wanted just to do the things that got them the higher grade, and as a result or as also an additional impetus to that is that many of the faculty dropped even any attempt at introducing creativity in the curriculum.

HATHAWAY: Just kind of bowled over by the students, you think, or just kind of almost throw up their hands.

HANNUN: Well, probably in the attitude of "Well, if they're coming here for the grade and they're not interested in very creative lab work or spending a summer in research, why bother with it? Just give them the didactic lecture."

HATHAWAY: And the problems at the end of the chapter.

HANNUN: Yeah. Something like that. So throughout, there were very few opportunities for basic research.

HATHAWAY: Or just even to see it happen. You say you entertained the thought in high school-- If I can just back up a little bit and get a sense of this, I think it's interesting. And this guy, who turns out to be somebody you have respect for and who really had an influence on you, didn't do anything for you then. What was your sense of your exposure to this idea of academic research and an academic career? I mean, was it really just that opportunities were limited for these people in Beirut? I'm trying to get a sense of-- You knew the possibility was out there, but there was almost no way to grab onto it and experience it for yourself.

HANNUN: Yeah. Absolutely not. I know now we recruit undergrads and high school students to spend a summer rotation.

HATHAWAY: They're more of .a nuisance than a help, right?

HANNUN: Well, they get to see what the lab is about and how science works. I think the ones who have come to my lab, the way I could see how they reacted, they had a positive experience. That to me is significant because leaving an impression on high school students that science can be a very gratifying experience-- We didn't have any of those opportunities, primarily because they didn't really exist as role models either. So research was as much of an abstraction as anything else.

HATHAWAY: As you say, as the medical school kind of rolled along, the clinical stuff became the real-- I mean, that was no longer abstract at all.

HANNUN: Yeah. Exactly.

HATHAWAY: I wanted to go back to that, unless you feel I'm kind of pushing you to answer my questions, as opposed to treating this area as a whole. I was also interested in getting a sense of how you compared the kind of clinical practice you got in medical school and your father's. You know, your father didn't serve for you, at first at least, as-- Well, I mean, I think a lot of the reason some people are doctors when their fathers are physicians, something about it excited them or they liked the big car in the driveway, if it's an American situation. I was just wondering if now, seeing this clinical stuff and patients and dealing with patients and finding that exciting, whether you were able to make some sort of connection with your father's work that you hadn't before or whether still he was doing such basic kind of triage out in the--?

HANNUN: No. I think I did. I definitely connected with what he did. We could discuss things, talk about things. Maybe I failed to express that. Medicine was probably to me much more viable than engineering because he was a good role model for that. And dealing with people, maybe I thought, maybe subconsciously, was a better career than dealing with concrete, for example. So there was this positive influence there.

HATHAWAY: But as you said, it wasn't the drawing card to go into medicine, which maybe you could see later on.

HANNUN: Yeah. It wasn't as such. I don't really recall ever sitting down and discussing with him those options specifically.

HATHAWAY: You said once they realized you were doing the school work, it was hands off. And who knows, maybe in some ways that's a really good way to deal with it. Your father never forced you to talk about what you wanted to do and said, "See, isn't this great, I'm a doctor. You can be a doctor." It was almost like, "Okay. You're going to be a doctor. Fine."

HANNUN: Yeah. Pretty much that way.

HATHAWAY: Maybe in the long run it paid off and you found medicine to be-- Who knows, he could have turned you off from it by pushing it. I'm just curious about this. For all he seems to have been hands-off, there seems to perhaps be a lot in the way of influence that, as you said, maybe you hadn't--

HANNUN: Yeah. I believe in sort of a more philosophical point of view. Children are more influenced by the reality of the situation rather than by how their parents try to fake it out to them. If your father tells you, "Go ahead and become a physician," and nags you to death about it, but you could tell that he didn't care a bit about being a physician himself, that's--

HATHAWAY: That's the key.

HANNUN: Yeah. And on the other hand, I've seen my father being not necessarily a workaholic but a very hardworking person. It must have influenced me in respecting that quality. I would consider myself a hardworking person. I mean, I take my work seriously. may be very cynical at many times, but I take my work seriously. I think he has the same attribute. But he never--

HATHAWAY: Said you had to have those--

HANNUN: Yeah. At all. But that's where I think children learn from their parents. If you see your parents acting as good citizens, you grow up to be a good citizen. If you see them not acting as good citizens, no matter how much they tell you to act as a good citizen, it's not going to stick. That applies to maybe the hidden positive reinforcement of working with people and being a doctor, not only as having a professional and secure job but also as having a rewarding kind of job. think that maybe, in talking a lot about the educational part of getting there, that may have been missing. I could see that if I was to be a physician I would have something I would like to do, dealing with people and trying to help them out. But even at that time, I didn't have a good concept of what it was. Actually, when I found what it was, it was even better than what I expected.

HATHAWAY: And perhaps it's something that, even if your father had dragged you out there once a month or something, you still wouldn't have got it the same way as you did by—

HANNUN: Yeah. Again, my perception from looking at my father very indirectly was a physician is someone who just prescribes medicine.

HATHAWAY: And reassures people.

HANNUN: Yeah. From the outside you just see that kind of interaction, the final action. You don't see any of the activity that's gone into providing this action. So that per se was not a very positive influence. I guess that's when I was on the wards and finding that "Hey, you go in and take a history and do an exam and read about things and think about what studies you want to get, what X rays. You have a differential diagnosis to think about and a line of management to institute." I found that this was extremely gratifying.

HATHAWAY: Can you say why--? This is as good a time as any. I mean, you've described almost a kind of-- This one's abstract. We don't have a particular case--maybe you do in your mind--but we're talking about a case. And the whole process you've just described, I think, from the beginning to solving a problem, or maybe not solving it well enough, but trying to solve it, and then to making sure that the problem stays solved or reaches some resolution, which is really what a doctor does in providing health care, right? Nurses take care of the day-to-day things and then actually kind of act as the foreshock. They get the message first, but it's the doctor that's expected to see the whole picture. Do you know why that's what grabs you? Because it's complex? Because it's got gratifying results, and it gets better usually?

HANNUN: Well, it's sort of a whole, on the one hand, social microcosm. On the other hand, it's a whole scientific microcosm. I think I may have to come back to that second analogy, the analogy between science and clinical practice. But it was a very intensive experience at the human, social, scientific, personal level. It was way much more than—

Remember, back then what I would see-- When I was very young, my father might take me to his clinic sort of as a baby-sitting arrangement for an afternoon or something and put me in the side room to read something or whatnot while he was seeing patients. That's when I described that I'd only see that he was dispensing a medicine but not seeing what was going behind it. Even that to me was still positive. But when I saw that what was behind it was much more than that, that was very gratifying. And again, back then, to put you in context, there were hardly any sophisticated television programs on physician role models and all the processes of things that could go on in a hospital or in a clinic. So I liked it. Basically, the bottom line is once I hit clinical medicine I liked that a lot. However, I think I liked it a little less and less as I progressed in it.

HATHAWAY: Less challenging or same old thing maybe?

HANNUN: It became less challenging. There was sort of an exponential growth phase in one's knowledge in understanding clinical medicine. But then with time that really plateaus and--

HATHAWAY: Even in the kind of changes that take place so rapidly, I guess.

HANNUN: Yeah. I mean, in terms of there's a major buffer that slows down things in terms of when they come to clinical practice. So clinical practice doesn't move as fast as I like it basically. But at least hitting the clinical years, I was very happy, and I was very involved. I knew that that's what I wanted to pursue at that time. So if you want to move on with the career choices, science at that time was intriguing. It wasn't a career option for me at that time.

HATHAWAY: From this practical side of things, about something to fall back on, always being able to pick yourself up no matter where you landed, that sort of thing? Or just also from the intellectual--?

HANNUN: Well, that sort of thing-- The problem is even at the intellectual level I did not have the opportunity to explore what that was at an intellectual level. And the only—

HATHAWAY: So this young M.D. who came back [Sahyoun], there wasn't any progress made or there wasn't something he finally was doing in the lab that really was going to go anywhere.

HANNUN: Yeah. When I was in the first year of medical school, he stayed a few months in Lebanon and then went back to Hopkins. And then--because that's going to come back to the story--he came back to North Carolina. You know, he didn't set up like the hottest scientific lab in Beirut. That wasn't physically possible. I did not have a visual model of what that could be about.

HATHAWAY: And it wasn't long-term enough to kind of follow something through—

HANNUN: Yeah. It did raise my interest. I became aware that "Hey, there is this dimension to medicine." started reading beyond the clinical literature, and the more the clinical literature became boring, the more the basic science literature became exciting.

HATHAWAY: Can you give us--I always say "us" because I always assume there's certainly not just an audience of one--what some of that was? I mean, do you recall? Was this just textbooks you came by? Was this the latest journals coming to--?

HANNUN: Let's say even starting the third year of medical school I was reading the New England Journal of Medicine and Lancet and a couple, of other medical journals. I was totally intrigued for maybe a couple of years but then much, much less with time. Now when I pick up the New England or Lancet, I dispense with them in fifteen minutes. I clearly remember the first time or even for the first few months I could spend the whole afternoon with the New England Journal, just being fascinated by—

HATHAWAY: It's like learning a culture from reading-

HANNUN: Yeah. Like learning a new language basically.

HATHAWAY: Sure. And how things get written about and who's who even.

HANNUN: Yeah. Where were we now?

HATHAWAY: I was trying to get a sense of-- I don't think I was actually engineering to see how you got away from the clinical to the stronger--

HANNUN: Initially, it was just sort of minor excursions into the basic research area. Maybe start with a review that the New England Journal throws in every now and then about something more at the basic level or maybe pick up Science magazine and look at it more than anything-- I mean, not anything deeper than that.

HATHAWAY: Not PNAS [Proceedings of the National Academy of Sciences]?

HANNUN: No. Nothing more specialized or less general. But clinical medicine stayed as a very strong influence with me throughout my internship and my residency. The other thing that was starting to come up as a career choice is subspecialty training. Throughout medical school you decide on what specialty training you want to go into. I went into internal medicine as the most direct, sort of, where you communicate with a patient, you know, where you try to probe the patient. That was the most gratifying part of medicine for me. As compared to surgery or ob-gyn [obstetrics-gynecology] or something like that, internal medicine obviously was a clear-cut choice for me, where if you got a good history from a patient, you could almost solve 80 percent of the problem. But you only could get a good history if you could probe the patient real well and get to the heart of basically their soul, you know, to really understand how they think.

HATHAWAY: Like this.

HANNUN: Exactly.

HATHAWAY: I get a little more time. It's not quite so vital to get--

HANNUN: To get the info real quick. So internal medicine was a very obvious choice to me. In fact, I hated surgery. I think surgery selects the morning people who are the doers, you know, the

people who have to be on the go all the time and don't really want to stop and--

HATHAWAY: Technical prowess and--

HANNUN: Yeah.

HATHAWAY: And the person that they're dealing with is unconscious.

HANNUN: Yeah. Exactly. I was turned off from all those and stuck with internal medicine. When it came to internal medicine, obviously the norm was-- There was a possibility to stick with that and then go out and practice, but by that time the civil war became rampant and Lebanon was not a viable option at all. And to me Jordan was never really an option. I didn't like Jordan as a country to live in.

HATHAWAY: Your parents weren't going to budge. I mean, they still weren't talking about leaving.

HANNUN: No. They became too entrenched in Lebanon.

HATHAWAY: And your sister [Rasa Hannun Bibi] and your brother [Imad Hannun] were already away at school somewhere else? Or your brother is at Caltech [California Institute of Technology], but I don't know if that's after.

HANNUN: My brother had come to Caltech by that time. He did engineering at the American University of Beirut but then went to Caltech for his Ph.D. Then my sister, she was the youngest, so she was still starting. She was in economics at the American University of Beirut.

Going back to the previous question, that's been an ongoing evaluation ever since for me--what are viable options in the Middle East? And really nothing has stood out in terms of a viable option.

HATHAWAY: For doing what you're doing here at Duke [University Medical Center]?

HANNUN: No. Even before that.

HATHAWAY: I guess I thought you were still talking like in the present tense, though, as well.

HANNUN: It's still ongoing because I still have both hats, I mean, clinically and scientifically.

HATHAWAY: And both citizenships.

HANNUN: Yeah. Exactly. Both citizenships, Jordanian and American. Nothing really stood out. I couldn't go to the West Bank, because I did go to the West Bank under the Israeli occupation once or twice, and it's too demeaning to-- I mean, I respect the people who live there under occupation. This is their home. They were born there; they grew up there. It's their home. They have to take it. I respect them for that. But I just can't see myself taking that as a way of life.

HATHAWAY: Looking forward or picking that as the-

HANNUN: Yeah. And Jordan wasn't really a viable option for me. The whole Middle East-- I did once in my residency go to one of the [Persian] Gulf states, Qatar. I think it would be spelled Qatar.

HATHAWAY: That's I think how we spell it here in the United States.

HANNUN: It was sort of like a locum tenens, spending two months as an internist there, and I hated it.

HATHAWAY: Just no culture in the sense of something you were familiar with?

HANNUN: I just didn't like the whole gulf area basically. Very wealthy people, born into wealth, without having had anything to do to earn it, and importing all expert and technical support from outside the country to run their hospitals, their schools, their police, their army, I mean their whole life basically. It was evidently clear to me that that wasn't a society that I could at all thrive in or be happy in. Although that was an option for many other people to go-- Definitely many of the engineers ended up in the gulf area, my classmates or whatnot. Even some very few of the clinicians ended up there. So the Middle East was not an option to practice in or that was an attractive option to practice in.

The only options there would have been at significant hardship that maybe I just didn't want to-- I didn't feel like-- I mean, the hardship in terms of uncertainty about the future, you know, whether you want to stay in Lebanon, Jordan. Look at Iraq now or probably Syria a few years from now. I mean, the uncertainly is just too great. And definitely professionally the careers were-- It would have been downhill from that point on, definitely downhill. So careerwise it wasn't attractive. And societywise it wasn't very attractive. As we talked the other day, I just didn't feel comfortable in a culture that doesn't respect you for what you are. That may respect you a lot for where you come from, may respect you for your title--"Oh, doctor," you know, that's tremendous--but not really what you do yourself. It's the title. It's your social status that becomes more important.

HATHAWAY: That's a very kind of American-- I mean, ideally. I'm not saying Americans are wonderfully democratic, with a small d, all the time. I think we hold that ideal up to ourself that it doesn't matter what your last name is.

HANNUN: Oh, that's like night and day coming to this country. That's again the reason that--

HATHAWAY: I'll let you say that we're great! I don't want to appear to be some yahoo on tape. But I mean it's an ideal of our society.

HANNUN: Well, it's a definite point of contrast. That's what made it very difficult-- Again, I'm anticipating myself here. It makes it very difficult once you come here to go back. That's not only my case but many, many other of my classmates and people who preceded me. And people who came after me find it very difficult too, because again you're selecting for people like myself.

Now, going back to my story, after internal medicine I wanted a subspecialty. I was very impressed with oncology, medical oncology and hematology. Those were mostly presented as a combined specialty training.

HATHAWAY: All over--? I mean, wherever you were looking, not just the United States?

HANNUN: I looked only in the United States.

HATHAWAY: Right after your brief experience in the gulf and you weren't even entertaining--

HANNUN: I wasn't interested.

HATHAWAY: And Europe was just not a--

HANNUN: Europe wasn't an option. We had many graduates come to the American University from European schools, and we were never impressed. They sort of follow the professor mode of medical education. That's how they operate in Europe, even in biomedical research. Very recently the Germans have broken out from that mold, but It's really the big professor who runs everything. Until that professor retires, you can't be very creative on your own. It's a very different-- And it's the same thing in clinical practice. So for subspecialty it became very obvious that the U.S. was the place to go. That's where most people had gone before. It was definitely important to explore that, and that's what I did. So I came here on a trip during my residency. I came here to Duke.

HATHAWAY: This was not your first trip to the United States.

HANNUN: No. That was my first trip. That was in '81, and that's when I spent three months in the States.

HATHAWAY: All down here in--

HANNUN: Mostly down here. The first two months all down here.

HATHAWAY: You can tell I'm from the North--"down here."

HANNUN: Yeah, down here.

HATHAWAY: Here in North Carolina.

HANNUN: Let me remember the details here. I did an elective in hematology here. The reason I came here is that friend I talked about.

HATHAWAY: We should maybe get his name.

HANNUN: His name is Naji Sahyoun. He had moved with his mentor, Pedro Quatrecasas, from Hopkins to Burroughs-Wellcome [Company]. Because Naji was here, he had made it easy for another person [George Atweh] to come to hematology at Duke. So that person became my connection later.

HATHAWAY: And this was a faculty person at American University.

HANNUN: No. He was training in hematology.

HATHAWAY: Just doing it before you did.

HANNUN: Yeah. Before I did. And when I wanted to explore places to look into, he said, "Hey, come try an elective, come look at this program." It works both ways. I get to see what hematology/oncology is all about, and they get to see me and see if-- You know, because, remember, especially for Duke at that time, a foreign medical graduate was almost an unheard-of entity.

HATHAWAY: This is '81.

HANNUN: That's '81. I mean, there were a couple of—

HATHAWAY: That wouldn't be the case, would you say, like out West or up in New England or down in Florida. I mean, I'm just thinking, is that--? Or Vanderbilt [University] even.

HANNUN: Oh, it would definitely be the case in Vanderbilt. I don't know the answer to that. Things have changed in the last couple of years, but in the eighties and seventies you would be very hard-pressed to find many foreign medical graduates.

HATHAWAY: I'm thinking of just-- And there is nothing statistical or scientific about this. But I'm thinking of Georgetown [University]. Again, this is all personal experience and graduating from there in '81 but actually doing work-study in the medical center. And then having contact with the UCLA medical center [Center for Health Sciences] again, '82, '83. I got a sense that there actually was a pretty typical situation for residents and beyond who hadn't done medical school necessarily in this country but were here doing-- And not just in public health.

HANNUN: So you think there were a few foreign medical graduates.

HATHAWAY: That it was accepted and nothing radically new about it, but maybe that's just--

HANNUN: It very much goes by the institution and maybe even much more so by different programs in the institution. Because now, for example, the program in internal medicine at Duke has a significant number of foreign medical graduates, many of them from my alma mater, from the American University.

HATHAWAY: I take it this person [Atweh], this friend of yours, kind of opened up not a floodgate but certainly a gate.

HANNUN: Not a floodgate. It started out like a trickle. I came to an elective here. My wife [Ling Obeid] came for internal medicine. We weren't married at that time, so I was here by myself in '81. I liked the program here a lot. I got to know the people; they got to know me. They offered me a fellowship position. But also the chief of hematology at that time [Wendell Rosse] offered to support me in looking at other programs. I looked at a few other programs in the States, other programs in hematology. The only other one at that time I looked at seriously was Stanford [University]. But I guess-- No, wait a minute. I came back to that the following year. So I came on another visit.

HATHAWAY: Like a three-month--

HANNUN: No. Shorter even, probably three weeks, in '82.

HATHAWAY: And when you say to support you, what you mean is that--

HANNUN: You know, help me go and talk to people, things like that.

HATHAWAY: He was extending his judgment of you not only to himself in getting you in his department but to anybody else.

HANNUN: Exactly. Yeah. I obviously liked the Duke program a lot, and that's what I decided to come to. At that time I had gotten engaged, and my wife came to Duke.

HATHAWAY: You met her here.

HANNUN: No. We met in Beirut. She had gone to undergraduate school at Rutgers [University], but she came back to American University in Beirut for her medical school. She was two years behind me. So when I came for a fellowship, she came for a residency. Again, in my fellowship here, the way it was organized, the first year was clinical hematology and medical oncology. I liked that a lot, but during that year it became obvious that beyond that first year of clinical subspecialty training, really there wasn't much more in terms of education and learning and--

HATHAWAY: What about teaching and the academic or the medical balance?

HANNUN: There were some possibilities for teaching, and it's something that probably I could have considered as an option, but teaching's never been a very valid option in the States in academia.

HATHAWAY: But I meant taking an academic appointment. You've got one, I realize, but I guess I'm looking at the difference between being a clinical professor and actually being somebody who is a PI [principal investigator] and running the lab. Maybe that distinction is in my own head and not something you're thinking about. But I was saying a more straightforward clinical kind of-- To go on and just stay at Duke and be a clinical professor.

HANNUN: Yeah. What I was trying to say is that the modes of-- I mean, obviously, again, let me put it that way. First of all, my career was going to be in academics. I mean, I had settled that issue. I wasn't going to go out and practice. Now, in academics, what I was trying to say is not only there aren't many role models for teaching but it's not something that's much valued either.

HATHAWAY: Absolutely.

HANNUN: I was trying to say, when I first joined the program here, I could have considered a teaching academic position as an okay model because that was the predominant model back in Beirut. But it wasn't a model that was much viable around here. And the other model would be a clinical researcher or a very active clinician in an academic setting versus a basic researcher. And that's when I started-- Again, intellectually, I think I really could see how clinical medicine had hit the plateau for me. There wasn't much more to learn from clinical medicine. And from there on the choices were either stay in clinical medicine totally--and, again, it's the same downhill analogy--and just execute, you know, having learned your vocation, then execute that.

Yes. There are some advances every now and then.

[END OF TAPE 3, SIDE 2]

HATHAWAY: You were talking about seeing kind of the plateau or the end of the plateau.

HANNUN: Yeah. At that time, I started thinking more seriously about trying my hand out at basic research. Obviously, the opportunity was there in terms of the way the fellowship program was structured in that the first year was clinical but the second and third years were very flexible in terms of either pursue more clinical work or clinical research or basic research. I spent quite some time during my first year in the States thinking about these possibilities. From that point onwards, I think basic research started growing on me quite fast. I started reading more--

HATHAWAY: You started reading PNAS [Proceedings of the National Academy of Sciences].

HANNUN: I'm trying to remember if PNAS specifically. The thing is something like our specialty journal Blood or Cancer Research. They are also more heavily involved in not just clinical research but also basic research.

HATHAWAY: And the bridge sort of--

HANNUN: So that was a bridge. Couple that to Science, maybe an occasional look probably not even at PNAS but definitely Nature and Science. And then sort of finding the excitement that was going on in the early eighties in basic biomedical research.

HATHAWAY: And in particular in oncogenesis? Or was there--?

HANNUN: Particularly in oncogenesis. Over the years that became more sort of cell regulation in general and how cells work.

HATHAWAY: That's kind of that other area of-- I guess a lot of the in vitro stuff was really being done as kind of developmental biology. They kind of met. That's '83?

HANNUN: Well, many things were coming together in that period, and I started becoming more

excited about that. That's when I thought, "Well, maybe I should take my research options seriously and try my hand at that." That's what I did. I don't know if you want to go into that today.

HATHAWAY: It's really more up to you if you want to begin with it. I would think that this actually is not a bad place to stop since it's midnight, and I'm sure you have a long day ahead of you. Why don't we turn it off now?

[END OF TAPE 4, SIDE 1]

[END OF INTERVIEW]

INTERVIEWEE: **Yusuf A. Hannun**

INTERVIEWER: **Neil D. Hathaway**

LOCATION: **Duke University Medical Center**
Durham, North Carolina

DATE: **1 April 1993**

HATHAWAY: We kind of left off really with your first couple of months here in Durham [Duke University Medical Center]. We talked a little bit about also just meeting your wife [Lina Obeid Hannun] and situations like that. I guess we've decided off tape to just kind of jump right into the basic research that you started doing. One thing you had mentioned on tape toward the end of our last conversation was your sense that you were kind of losing a sense of being challenged with medicine. And actually, one of the things that you mentioned to illustrate that was reading the journals. Whereas in the beginning of your medical studies you'd take hours to read JAMA [Journal of the American Medical Association] or Lancet or something like that, you're now able to open it, get the four things you needed to know out of it in ten minutes, and set it aside. I was interested in the fact that you really became acquainted with a lot of basic research and with what was going on in biochemistry or molecular biology through the literature. It seems that a lot of maybe your, quote, "exposure" was that way, and I was wondering if you had a-- Certainly you've talked about the young man [Naji Sahyoun] who returned from I think it was Duke but who went back to--

HANNUN: Yeah. He was at [Johns] Hopkins [University] at the time.

HATHAWAY: Excuse me. I also have kind of an idea of where else you got kind of-- "Exposure" is not the right word, because it wasn't in a lab, but I guess I would like to kind of make that have some connection with the last conversation, last time's conversation, but also just to get a--

HANNUN: My exposure was primarily the courses I took in first-year medical school. Biochemistry really stuck in my mind. I still to this day remember almost everything I read in biochemistry that year. It was probably the only course during first-year medical school where I did a lot of outside reading too. I enjoyed that a lot and talked a little bit about that. My other exposure in Beirut was two things. One was in clinical research. told you the other day, too, I mean, I sort of always felt inclined that I was going to end up in an academic situation rather than in a clinical practice. Obviously, the two outlets were either clinical research or basic research. I tried to work a lot on clinical research, and in Beirut that was possible. For example, for one year on the side I collected material on maybe four hundred patients with rheumatic heart

disease and analyzed that and collected a lot of data and analyzed that a lot. It didn't make me feel very happy. I didn't find that I liked that a lot.

HATHAWAY: It was boring work or—

HANNUN: It was tedious work, a lot of data collection. It's what you mentioned a bit ago, a retrospective analysis. And that kind of clinical research just didn't click with me. I did try a little with Naji Sahyoun when he set up his lab, try a couple of research projects with a very cursory type approach to a biochemical project. Again, I didn't like that a lot, specifically at that time. It didn't convert me, but it did open my eyes in terms of how difficult it was to obtain new knowledge in biomedical sciences. That to be able to contribute even the smallest item you had to read a lot, find out what's known, how things got to be known, how to set up an experiment to start adding to that, and how difficult it was to do that.

In Beirut it was almost impossible. I mean, by the time you order, let's say, ^{32}p ATP [radiolabeled adenosine triphosphate]-- By the time it got there, it's been through at least one half-life. So it did teach me a lot about improvisation in research, having to set up your own tools and maybe deviate from well-established methodology because of the lack of the appropriate or the most convenient reagent. But it didn't convert me in terms of saying, "Hey, I want to become a basic scientist."

HATHAWAY: What was it that you were working on, or trying to work on maybe?

HANNUN: One was to try and-- God, I have to remember that. The one thing I tried my hand on was to look for adenosine and ADP [adenosine diphosphate] receptors on blood cells. At that time that was pretty novel. But we didn't get far along with that.

HATHAWAY: And that was more a materials kind of-

HANNUN: A lot had to do with materials. In retrospect, a lot had to do with that I didn't just prepare well for those studies. I mean, I was basically taken off of the street and thrown into this situation. As I mentioned before, there was no preparation in terms of practical experimentation, period, in my education.

HATHAWAY: And so, in a sense, you and-- I guess from what you're saying there were two or three other people involved. It was just a matter of giving it a try really. And with this one guy back from Hopkins, Naji. That's his first name. I don't mean to be so informal with somebody I haven't met.

HANNUN: Well, he has passed away, actually, a young man who passed away recently. He died of cancer, a very bad malignancy. He was a very bright person. He was very excited about science. That definitely got transmitted, not just to me but a whole chunk of us in medical school.

HATHAWAY: But there was some frustration with the conditions in—

HANNUN: In the lab. Yeah.

HATHAWAY: I mean, you say you didn't get far, so I assume that means--

HANNUN: Yeah. I wasn't much frustrated because I didn't have much expectation from it either. I mean, I wasn't going there and saying, "Hey, I'm going to accomplish so much in those two months." I just wanted to see what this was all about. I mean, I had to learn how to handle pipettes and radioactivity and scintillation counting and whatnot.

The other thing is we toyed around-- He [Sahyoun] was very interested in neurological diseases and neuropharmacology, neurobiochemistry. We sort of started on a more hypothetical project at that time in terms of trying to understand multiple sclerosis. I say "hypothetical" because we did a lot of reading, we discussed many ideas, but it never came to the point where we said, "Hey, we're going to devise this experiment or that." So it was a couple of months that I enjoyed quite a bit, but it did not convert me at that time.

HATHAWAY: Just two kind of quick questions, not expecting that they'll necessarily lead to anything of real great import. Where did the money come from to buy or at least try to order them, even if they showed up kind of, how shall we say, half dead? That's not necessarily a good pun.

HANNUN: I think the money came mostly from departmental sources. I think at that time the department and university were trying to get Naji back to a more permanent position. So it was like a pre-startup, something for him to have a lab and see if he could work. And I think he approached it, too, in terms of a trial, whether research would pick up and flourish or it was going to be working against the odds. I think he settled down towards the latter conclusion. But I think the money came from-- The space definitely came from that, and the money probably came from that.

HATHAWAY: And your interest in the MS [multiple sclerosis] was just--

HANNUN: It was mostly Naji's interest. He maintained that working in sort of neurobiology mostly, at the biochemical, molecular level.

HATHAWAY: I just thought it was important to get some sense of-- Again, not that these are all directly connected or anything like that, but just I guess kind of your experience. And then I would, I guess, kind of jump ahead and ask, how did it come about here that--?

HANNUN: My next encounter with research-- Actually, when I came to Duke in '81, I did I think one or one and a half months of clinical work. I liked that a lot, by the way. I liked the academics a lot at Duke. People were extremely knowledgeable, very nice people. I liked that a lot, so much so that when I went back to Beirut I tried to--because I was to become chief resident in medicine there--install some of those things I learned. But I also spent two to three weeks with Russ [Russel] Kaufman, who now is actually the chief of hematology here. He had just come back within a year or two from the NIH [National Institutes of Health], where he had trained with Art [Arthur] Nienhuis in molecular biology. So to me that was a whole new area of doing DNA work and whatnot. Again, the expectations on my part were not high at all. We just wanted to look at genomic DNA from patients with thalassemia. So it was, again, learning the very ABC's of DNA extraction, running gels and enzyme digests and whatnot. So my expectations were not high., I didn't give it-- Actually, no, I did spend a lot of time reading. That's always been my approach: before I get into something or as I get into something to try and get as solid a background as I could. So I did spend a lot of effort in trying to understand molecular biology.

HATHAWAY: In a sense, then, you hadn't really had any kind of formalized classwork that was really strictly geared toward molecular biology versus--

HANNUN: Exactly. That was very novel at that time. I think Russ Kaufman was considered the only molecular biologist probably at Duke at that time. Maybe I'm not correct on this, but definitely in the Department of Medicine he was the only person who could do molecular biology. It was very novel. It hadn't yet filtered through to the curriculum, even in the States.

So that was another encounter with research. Maybe it more opened my eyes again to another kind of research, more in terms of the pace of research, also what it takes to get research done. I would consider both experiences up to that point to have been negative experiences in terms of achieving any meaningful results. But again, that was valuable experience in terms of expectations, to have realistic expectations, in terms of how to judge a project, whether it was going to be useful or not long-term, you know, worth the investment or not. It's very different from seeing patients, where you go through the process many times a day. Anytime you pick up a project, it's a long-term commitment. You better choose a good project.

HATHAWAY: You said three weeks of clinical, four weeks, or am I missing and thinking of the three months that you were here?

HANNUN: I was here at that time for three months. It was partly in clinical work, which I think was like a month and a half, maybe actually closer to two months or eight weeks in clinical medicine, more like two to three weeks in the lab. And then a couple of weeks, one or two weeks, I just vacationed basically.

HATHAWAY: In a sense, in two weeks, just from walking into a lab or an operating lab, you kind of were able to, again, see these things, like see how much work went into a project or how many people were working on it, to understand some of the-- I mean, obviously you've been doing reading, but that actually seems to me a pretty quick study. To get that kind of information out of something in two weeks, that's actually kind of a high payoff. I mean, you're not going to walk away with a disappointed or--

HANNUN: Yeah. But I didn't even learn significant skills from that. I mean, these are really primitive, elementary skills. You have to look at me in terms of someone who had very little research experience. And I can see it now in high school kids who come to my lab or undergrads, who I can structure for them a more productive experience in the lab than I did.

HATHAWAY: In these two weeks, you mean, not when you finally came back and worked with Dr. [Robert M.] Bell.

HANNUN: Yeah. The other benefit from both encounters was in both cases I had invested a lot into reading in new areas at the basic level.

HATHAWAY: What were the areas, and why--?

HANNUN: One was receptors, the other was multiple sclerosis. But that turned out to be very confusing. I think the literature on multiple sclerosis is still very confusing. You can't make head nor tails out of multiple sclerosis in terms of the basics. Is it an immune disorder? Is it a whatnot? The other in terms of reading in molecular biology. So it became easier to pick up like Science and start to appreciate what the authors were trying to do and to say in their studies and to be really impressed by the work.

HATHAWAY: Or perhaps critical of something you thought might be--

HANNUN: I wasn't that advanced, I think. I couldn't critique something real significantly. I probably couldn't even read a Science article like from A to Z and figure out exactly what they were doing. I wasn't that sophisticated, but I could get a sense of where science was at. Those were very exciting days, which we talked about a little bit the other day too. During my clinical year--if you want to spend just a couple of minutes on that--that was a very tough year. I don't know if we talked about that or not.

HATHAWAY: I think what we talked about was your reception here. You were talking about your year here and those sorts of things, as opposed to any clinical work you did or what it was like.

HANNUN: Well, it was a tough year, a very rough clinical load. That's how hematology/oncology is. It's a very wide specialty, and you have to master it. And we had to master it in one year. Fellows still have to do that. So it's a very intensive year. The patient material is very intensive too, emotionally and physically, especially on the oncology side. We were more or less in a new country. We were newlyweds, and both were-- You know, my wife was an intern back then, and that's even worse than being a fellow in hematology.

HATHAWAY: And she was an intern--

HANNUN: At Duke, an intern at Duke, in the Department of Medicine. Yet with that I still tried to keep some contact with what was going on in basic research. My research contact person at Duke at that time was Jim [James E.] Neidel, who went on to become I think senior vice president at Glaxo [Laboratories]. He was sort of the model of a successful basic researcher in hematology, a young, active researcher. I had talked to him before actually, when I was here in '81. That was the main reason I had come to Duke, because I thought that was exciting research or part of the exciting research. I had discussed with him options that year to either join his lab or structure something related to that. And my interest, coming from the clinical side-- Oh, I must add one more thing here for background. You came across that too. I did also some clinical research that first year. I looked at testicular cancer patients. Again, I found that to be tedious, ultimately boring, and it doesn't contribute much.

HATHAWAY: I was going to say, what was there--? In reading it, I was kind of not clear in getting a sense of how the retrospective study allowed one to then make decisions about treatments.

HANNUN: Not much. I thought the rewards were very few from those kinds of efforts. Now, to engage in prospective studies, that was a possibility. I must confess there weren't too many role models around Duke to sort of look into that. Again, with my clinical reading, I had come to the conclusion that clinical research was not going to satisfy me. The way it was conducted was we took one agent that's used in cancer and now tried to give it in three days rather than two or five. It was more splitting hairs rather than acquiring fundamentally new information. So I definitely wanted to find out what basic research, you know, more sort of longer commitment, what that meant.

Approaching it from that point of view, I was mostly interested in the hematologic malignancies. I wanted to study leukemia, biology of differentiation, what makes leukemia cells grow, what makes them differentiate. Jim Neidel at that time was studying leukemia cells, and he had made an important discovery concerning phorbol esters, which are tumor promoters, and possibly how they work. Earlier on, a group in Japan led by [Yasutomi] Nishizuka and [Yoshimi] Takai had discovered a new enzyme, a new protein kinase, called protein kinase C. They had shown that it really belonged in the signal transduction pathway. It was activated by lipids, by diacylglycerol. They had also shown that this tumor promoter activated this kinase. What Jim Neidel showed is that this kinase is actually the receptor for those phorbol esters.

Now, to put it in some perspective, the finding that this kinase was activated by diacylglycerol was nice. It had placed this enzyme in what has been called the PI [phosphatidylinositol] cycle of cell regulation. People had discovered that cycle in the fifties. [L.] Hokin and [M.] Hokin had discovered that cycle in the early fifties. In the early eighties, the two products of this cycle-- Diacylglycerol was found to activate a kinase, and the other, inositol triphosphate, released calcium from inside the cell and really initiated a lot of activity in the cell, biochemical activity. So that was good.

But the more dramatic, actually, biologic significance came from phorbol esters. Why? Because phorbol esters are tumor promoters. They were discovered as tumor promoters in an animal model of tumor promotion and cancer formation. But over the ensuing twenty or thirty years every cell biologist who tried phorbol esters in their cell system found that phorbol esters did something important in cell biology. There was no cell system that did not respond to phorbol esters by some important biology. So when Nishizuka found that phorbol esters activated protein kinase C and Jim [Neidel] found that protein kinase C is the receptor for phorbol esters, it was not like just something being hit by phorbol ester accidentally. It was it, pretty much. Then suddenly every cell biologist became interested in protein kinase C, and they still are. It's very true. It's the only kinase that's I think individually entered in the Index Medicus. The number of publications on the biology of phorbol esters or protein kinase C is too numerous to keep track of. So that really put protein kinase C in the center of cell biology research.

That's when I approached Jim Neidel in terms of the possibilities of working in that area. We had a couple of discussions. I think he sensed my determination to get into basic research. He was an M.D./Ph.D. He had a couple of recommendations for me. One was, if I wanted to become a basic [science] researcher and sort of be in that bridging region between the

very basic and something maybe with ultimately more clinical relevance, to actually train in a more rigorous fashion, to seek more fundamental training, either biochemistry or molecular biology. And so that was the first sort of outcome of those discussions. The second was, he was starting a collaboration with Bob Bell, who still is in the Department of Biochemistry at Duke, to look at diacylglycerol regulation with protein kinase C. Ironically, Bob Bell-- The collaboration started because Bob Bell was a lipid biochemist. And ironically, Bob started being a big skeptic that his favorite molecule, diacylglycerol, which he worked on metabolically, would do something in terms of activating a kinase. It just didn't fit sort of the way people understood lipids. It was this skepticism that actually led to a very healthy collaboration and understanding of how diacyiglycerol activates the enzyme.

HATHAWAY: Was Bell maybe even convinced--I mean without being completely convinced until he saw it happening in an experiment--that the connection between the protein kinase C and diacylglycerol would be more accidental or would have intermediates or this would be some minor--?

HANNUN: Yeah. He couldn't see how a molecule that's in the cell, as a metabolic precursor to all the phospholipids-- [indicating] This is diacyiglycerol there on the chart in the center and surrounded by all the phospholipids in the cell, and there are dozens of phospholipids. Diacylglycerol is really at the heart of all those metabolic pathways. That's what Bob Bell was working on. Suddenly to tell him, "Hey, we're going to pull that out of here and put it in the center of something very different--" I'll give you an example of how skeptical he was. Basically, he [Neidel] suggested that I explore working with Bob Bell, and I did that. think we hit it off real well initially. The arrangement was-- Bob Bell wasn't working with protein kinase C then. I went and spent a couple of months in the summer of '84 with Jim Neidel, learned how to work with protein kinase C, how to purify it and start doing some assays on it. The assays were real crude and obviously designed by biochemists with no expertise in lipids. The first thing Bob Bell wanted me to do was design an assay that's amenable to study lipid protein interactions. In fact, we designed a mixed micelle assay. But to give you a sense of Bob's skepticism-- Once I got the initial technical know-how from Jim's lab, I went to Bob's lab. The first experiment he wanted me to do was to make sure that I was activating a kinase and that there wasn't a lipid-metabolizing enzyme in the prep that was resulting in phosphatidic acid. He actual thought that the ^{32}p we were measuring was not in histone, the protein substrate, but in phosphatidic acid. So he wanted me to really make sure we were not wasting our time on that.

HATHAWAY: They weren't screwing up over in the other lab.

HANNUN: And we did that. Obviously, when you look at the data, it was phosphorylation of the protein. So we knew that diacylglycerol was activating this kinase. We designed this approach to evaluating mixed micelles. The success was phenomenal, because the very first experiment I tried worked. It's a nice thing, because that's the kind of approach where, in the

two months I was with Jim Neidel, I had again delved very deeply into the literature there. I came to know all this history I'm telling you about and more of the technical aspects of it. I could start to refine the assay and understand it more. When I went to Bob's lab, I spent a couple of weeks maybe or a week just studying methods of solubilizing lipids and developing these kinds of approaches. So it worked real well from day one.

HATHAWAY: I get a sense in talking with people that there is still some sort of, let's say-- That the actual doing of experiments is a skill, like I think anything that one does. You know, one builds houses or one develops these kinds of manual skills. I get the impression in talking to you that they're just already kind of there from whatever, just innate, or--

HANNUN: No. Technically, I've always been very careful but never brilliant. I wouldn't rank myself technically as a whiz, definitely not. But I've always been very careful, probably recognizing, actually, deficiencies in even my ability to hold tubes and pipettes. I'm not terribly great at that. But my experiments would work pretty well.

HATHAWAY: Because you're cautious. Step by step.

HANNUN: I'm careful, not to the point of being obstructive. I'm pretty efficient too. I've always probably been more on the side of being efficient, but I treat things with caution until I figure them out. When I'm comfortable with them, I would allow myself some more laxity if you will.

HATHAWAY: I guess I'm asking this not just because I wanted you to say, "Oh, I'm a klutz" or "I'm not" or "I was just born with it." I'm wondering if the way you approach the manual and day-to-day aspects of your work guides or has some influence on the kinds of work you choose to do. In other words, if you're not a whiz, do you tend to like the low-tech, basic end of biochemistry, where there are things that are always techniques that can be applied to a whole other set of experiments that you've already got a grasp on? Or are you pretty daring? Or do you encourage that--to try something completely new and go send somebody up to another lab to learn that whole new thing and just--?

HANNUN: The way I describe these things to my students is to tell them that as a scientist they're like artists, and they have to paint a picture or write a story. And it has to be a new story, a contribution that people can say, "You didn't just copy someone else's painting." Now, to do that and to come up with something beautiful, you have to be able to get your hands to do what your brain wants them to do. You can have people who can paint very beautifully, but if they don't have the right connections they can't paint what they want to express in painting. That's really what you want in science is the expression of your ideas in research through experiments.

And those connections-- I mean, that's where you have to develop those connections, understand what goes into developing and making those connections, because that's how you make a nonscientist a scientist is to give them those connections. Those connections come from reading, understanding, and thinking at all kinds of levels. You have to think about the technical level. I mean, you need to know that if you use different-sized brushes you get different results. And if you mix different paints differently you get different results. It comes from reading and developing more general strategic goals. So you can say, "Hey, I want to paint a picture of the sunset." You don't start painting and whatever comes out comes out.

Then you also have the intermediate level of tactical approaches towards science. Those probably are also very difficult to accomplish. Where you can say, "My approach towards painting the sunset is going to be to position the sun here, the clouds over there, the ocean from this perspective, and I want to include people in it." And the same thing with science. You have to say, "I want to study--"

In one case, we want to study if sphingolipids are precursors to second messengers. This is a big unknown. This is the big picture we want to paint. Tactically, what are we going to do first and next? We're going to look at metabolism of sphingolipids and see if there are any products generated under physiologic conditions. At the technical level, we need to be able to look at these sphingolipid metabolites and whatnot. So that's what I try to get my students to appreciate, that if you lack at any one of these levels, you can't translate the final image you have or the big question you're trying to answer into concrete data that will direct you one way or the other.

HATHAWAY: So I'm really kind of asking the question backwards. It's not about limitation or innovation on one thing leading to-- It's not unidirectional or something like that, I guess is what I'm-- I mean, you're describing something that's almost-- I don't know if I can even come up with a word or an idea that describes the approach, because it's obviously not theoretical either. It's not like, "I've got these great ideas and I want to find out the answers to them, so I will be driven by those four ideas and I will do them." There is some sort of reality check always--

HANNUN: Yes. You have to be able to execute at the very realistic level step by step. Yet you have to make sure that these experiments you're designing are answering the questions you're asking. And going now to the strategic level, you have to make sure that these are really the questions that you want to ask and that they fit some general logic or at least a logical approach. I think I've followed that. I've followed that very carefully with my students at all times. And that's where most students-- They all come defective in one area or the other, otherwise they wouldn't be students—

HATHAWAY: They'd be in charge.

HANNUN: Exactly. I always tell my students the time to leave or the time to graduate is the time that you feel comfortable that you can do science in this fashion. Some students come with very developed ideas about the areas they want to study and how that fits the universe, but then they can't translate that into experiments. So you have to make them take the strategy and devise tactics out of that. On the other hand, you get some students who are very good in designing experiments but then they can't analyze the data very carefully. They also need to troubleshoot. I mean, troubleshooting is part of this connection between the brains and the hands at the bench side. Troubleshooting also has to fit the general scheme of things.

HATHAWAY: Was this something you think you were aware of before you walked into these two labs here at Duke? Or was it maybe related also to clinical practice? Or is this something you've kind of learned from these two guys?

HANNUN: In retrospect, I can analyze this pretty well, I think. Developing my understanding of science obviously came as I stayed with science. But in retrospect it's obvious to me--and I try to make it obvious to all the medical students and the M.D.'s who come to work in the lab--that these are identical skills to those they use in the clinic. They go by different names, but they're identical skills. It's experimental problem solving. What we call in the clinic history and physical, here we call data collection. We do studies of the literature; you do studies of the literature here. You do a differential diagnosis in the clinic; here you call it hypothesis generation. They're the same mental functions. You order lab data and X rays in the clinic; in the lab you run your experiment to collect the data, refine your hypothesis, narrow down your differential diagnosis. The parallelism is tight, very tight. It's obvious, when M.D.'s come to the lab, they're able to hit the lab running much faster than non-M.D.'s.

HATHAWAY: You mean than a Ph.D.? Or you mean like an undergrad?

HANNUN: Like a graduate student starting out.

HATHAWAY: Okay. Who hasn't got lab experience.

HANNUN: A Ph.D. is someone who has gone through that phase. Yes. But that helps in allowing me to formulate what it takes to be able to succeed in solving scientific problems.

Going back to science--my experiences--I stayed in science because I prepared well for my important experiments. They worked easy, or readily, I should say. I was concerned back then whether this was what I wanted to do or not, even with the initial success. It's funny, because at that time I had a much more global aspiration of what I wanted to accomplish out of

science. Suddenly I found myself becoming the world's specialist on mixed micelles, and I thought, "I don't want to do that for the rest of my life. I don't want to be that kind of person."

HATHAWAY: You mean too narrowly focused?

HANNUN: Too narrowly focused. It's very funny, because in retrospect those skills have really defined my specialty for me. But at that time I just thought, "That's not going to satisfy me."

HATHAWAY: And I would suggest--not criticizing people who pick a narrower focus or, let's say, work or run a smaller lab--your focus really doesn't seem that narrow anymore. You can certainly talk about an area it covers and how it's--for me, at least--very clear why that has developed out of this. Just even from an armchair view, it's all pretty clear. But it seems to have expanded, not going in a straight line but also maybe poking around as well. And maybe I'm jumping the gun and talking about this before we've talked about the specifics.

HANNUN: Well, let me give you sort of the background to that, because at that time I didn't want to be a mixed micelle specialist. Now I wouldn't mind having spent three years just becoming that. It's funny sort of the perspective there. But at that time I wanted more out of science. And the first grant I submitted-- I was able to collect enough data and submit a grant proposal within three months after being in the lab for a Physician Scientist Award and actually got funded. Although, again, the material was pretty dry for anyone other than a lipid biochemist. So I was--

HATHAWAY: You mean straightforward-- I mean, I'm trying to get a sense of what you mean. You're kind of using it in a pejorative sense.

HANNUN: Dry?

HATHAWAY: Yeah. Just dull, you mean? Kind of that you didn't know what the answers were yet, but you knew—

HANNUN: I was proposing to do studies on mixed micelles and regulation of protein kinase C that at that time I didn't really appreciate their significance. And obviously I couldn't communicate that therefore in the grant process. It's all a question of timing. If I had submitted that grant three years later, it would have been considered the best grant in the world, and I probably would have been much more convinced about it. At that time, I thought-- You know, I was uncertain, thinking, "I'm not going to make a career out of mixed micelles. I'm going to use

them, though, to get my Physician Scientist." Because I wanted to give the lab more time than my fellowship permitted, which was two years in the lab, and the Physician Scientist would have given me five years. So I wasn't convinced about it. I definitely didn't communicate any excitement in my grant. It was a dry grant. It got funded, and it really relieved me from a lot of pressures in terms of "Hey, I'm funded five years. Now I can do whatever science I want to do."

And what I did was a couple of tacks there, take two different tacks. One is I wondered whether protein kinase C was a target to develop cancer chemotherapy. It was a very simplistic, almost naive notion at that time, but I spent quite some time looking at inhibitors of protein kinase C and using those sophisticated, more exact ways of analysis. I think that got actually Bob Bell very excited about protein kinase C. I mean, for a basic scientist, he found that this was a real opportunity to have relevance for what he was doing, especially coming all the way from lipid biochemistry, which was not exciting even to other biochemists. He got very excited about that, so much so that he set up a company to study inhibitors of protein kinase C, and actually he did that.

The other thing is Carson Loomis, who was in the lab at that time, was doing structure-function studies on protein kinase using some of the methods that I developed actually with his help. He found that one molecule did not work the way he thought. He was testing it. It was sphingosine. It was maybe inhibiting rather than activating. Somehow these immediately started a whole process going in my mind that here is this molecule sphingosine that's naturally found in cells that's interacting with this enzyme.

I didn't just ask what was going on here. I almost developed a full scenario from day one with that. The first thing I did was study it as an inhibitor, and lo and behold it was an inhibitor. But I developed a whole scenario that hasn't panned out yet. It probably will never pan out as such. But that's something I think I've always-- I bring that as an example. I've always been good at taking one piece of information and putting it in the best possible light as how that could possibly unfold as a long-term project. For example, with sphingosine I thought, "Hey, maybe there are signals on the outside of the cell that activate enzymes that break down sphingolipids. That generates sphingosine, that goes on to inhibit protein kinase C." I would say that entered my mind almost from the first day.

HATHAWAY: Why something like that? Was the relationship between the other lipid and the protein kinase C still novel? In other words, there wasn't yet a sense that all these lipids were now going to have all these other functions?

HANNUN: Oh, absolutely not. It was still an anomaly that diacylglycerol was a bioactive molecule.

HATHAWAY: Here, as you point out-- For the record, we're pointing to a rather complex and confusing-looking chart that you can find in one of the biochem books, too, I believe. It's got a

real central role in that. It's old-fashioned, if you will.

HANNUN: Yes. Old-fashioned central role.

HATHAWAY: The jump you're making seems-- Let me ask it the other way, since it didn't happen that way. Why would people still want to treat it--after maybe a good two years' worth of work--as an anomaly?

[END OF TAPE 5, SIDE 1]

HANNUN: It was an anomaly. I mean, even people who studied protein kinase C and were very excited about it, I'm absolutely convinced they were excited about it because of phorbol esters not because of diacylglycerol. And actually very few people have studied diacylglycerol as the molecule on its own, in its own right.

HATHAWAY: Because it's so--

HANNUN: It's a lipid. It's difficult to work with. People haven't made the realization that "Hey, maybe these lipids are there not just as building blocks for the membrane of the cell but that a lot of information is being passed through lipids." That has become now, currently, our sort of central thesis, that lipids carry just tons of information. That primarily their raison d'être is to transmit information, as relays of information. But back then diacylglycerol was considered as an exception or an n of one. So with sphingosine, actually, when I first told Bob Bell that "Hey, what about sphingosine doing that?" he was just as skeptical as he was with diacylglycerol and protein kinase C. Only after a few months, when I had a lot of data showing that sphingosine really inhibited, how it inhibited, and it inhibited in cells-- Actually, one of his students who was a sphingolipid biochemist had picked up on that, Al Merrill, Alfred Merrill. I discussed that with him, and he picked up on that and actually came up with his own study at that time. [Only then] Bob started becoming very interested about it. At that time, I think it became clear that these lipids are more active molecules than just metabolically.

You asked me a question about why is it not intuitive. I think now we can say it's very intuitive. Actually, you want to take a molecule like diacylglycerol-- If you were designing cell function and cell communication and signaling events, you want to take a molecule like diacylglycerol that's at the heart of so many metabolic pathways and use it also as a signal, because this way you make a very solid interface between a metabolic function and a signaling function.

HATHAWAY: As a matter of fact, as it's functioning in its metabolic way, it changes, and the way it changes other things is going to be the signals, right? I mean, in a sense, it's not doing two things. It's doing one thing, but of course it has a dual function.

HANNUN: It has a dual function. Well, maybe I should explain that. In the metabolic sense, the old metabolic sense, diacylglycerol was the building block to make other phospholipids. In the signaling function, totally dissociated from the metabolic function, it's a signal. If cells generate diacylglycerol, that's a signal to activate protein kinase C.

HATHAWAY: But it's also going to be making diacylglycerol do its lipid or its typical, old, metabolic function.

HANNUN: Now, I would still think currently, if you want to say "dogma"-- That's a funny thing about science which I never understand, is after being around for two years things become dogma, you know—

HATHAWAY: No. I do, yeah. I actually find it really very interesting.

HANNUN: It is very amazing. I mean, it's probably a tendency on scientists' part to simplify the processing of knowledge and the communication of knowledge because there's so much of it going on. I think dogma now would have it that these are more distinct, separated events, that diacylglycerol is a precursor to lipids. That's one function. And it's a signaling molecule. That's another function.

HATHAWAY: So maybe, let's say, in an evolutionary sense or in a gross cell biological sense, what's the order perhaps of it having--?

HANNUN: That's a good question. I would think in an evolutionary sense perhaps the metabolic function came first, and then evolution would say, "Hey, this is a neat molecule to carry a signal through."

HATHAWAY: Because it's so central or so busy changing and conforming.

HANNUN: It's central. And if you look at it in terms of signal, it's something that you want to reprogram cells with. That's what a signal ultimately does. You can obviously give it a kinase as a target, but also by changing all other phospholipids you're reprogramming cells too. So you

may want to take a molecule that's already at the heart of one metabolic function and give it another signaling function. That's almost philosophy of science at this point.

But in terms of my working, I could always--not always--but I find myself that I'm very good at painting a big picture. Maybe 80 percent of the time it turns out to be wrong. That's the way science works. That's sort of what I took with me when I left Bob. Well, before I left Bob, since I got my Physician Scientist, I took more formal training in science. I attended course work, and I started doing some molecular biology projects on my own, cloning techniques, because obviously it became apparent that you can't do serious cell biology and molecular biology if one didn't have the techniques and tools of DNA work and RNA work. So I sort of taught myself on my own those techniques while with Bob. I was very comfortable in my productivity because I had a technician [Linda Karolak] working with me at that time and I could generate a lot of data on my enzymology and mixed micelles and whatnot, while at the same time freeing myself up to do other things.

HATHAWAY: And that was, in a sense, your own money. This is by the time you had gotten that grant. So even though you were in Bob's lab and using the space, I mean really--

HANNUN: Well, I'm sure he supported the research with his money. I mean, my money didn't go far in terms of supporting research beyond my salary and a part-time technician.

HATHAWAY: Could we maybe just for the record-- Probably it's very easy to find what the grant was worth over five years.

HANNUN: I think the grant was somewhere around $60,000 per year, close to $300,000 over the five years, which covered mostly my salary, some of the technician's salary, and some supply money. Actually, it was structured in sort of two phases: the first phase, two years, would pay mostly my salary, and the third through fifth would pay for additional technician support and some supplies. So it got a little better.

HATHAWAY: But perhaps, although geared specifically toward M.D.'s with, again, this kind of developmental sort of thing-- This idea that "Okay, you'll be in someone's lab. There will be support there. But here is this, I guess we'll call it, hump money or whatever." You know, it's to get you over the-- And to build you up so that you can-- It's very programmed, but I guess it—

HANNUN: It's a brilliant program, this Physician Scientist.

HATHAWAY: This is NIH?

HANNUN: NIH. It was--

HATHAWAY: I believe some of your colleagues, M.D. colleagues, did it, too, and that's how they are—

HANNUN: It was designed I think by [James B.] Wyngaarden, who was chairman of medicine at Duke and went on to become head of NIH. I think he designed that. think that's one of the more successful programs at NIH. It has a very well designated target group, and it really accomplishes its goals with that target group because it allows physicians to commit to a career in research without having to worry about funding. It's a five-year grant, and it allows them to become junior faculty once they get it. It allows them to train, keep on training, and it really covers that transition period, because most physicians would get it after having spent some time, anywhere from a few months to a couple of years, in the lab. Instead of trying to set up something on their own and then fall on their face, it gives them this transition. To me, that was obviously a blessing because if I didn't get it back then, one, I would have been probably very disappointed. You know, I didn't have that sort of patience with a career in science back then. I wasn't very sure.

HATHAWAY: You'd have walked away maybe.

HANNUN: I may have walked away. And it definitely made my next phase very secure. I just worried about science, that was it. So during that tenure of the Physician Scientist, that's when I was offered to stay here at Duke as junior faculty and set up my own lab right here. What I wanted to do back then, my sort of strategic plan, was to say, "Let's take these studies to a cellular level and define sort of pathways of cell regulation at the level of the cell," using my background in enzymology, protein chemistry, lipid biochemistry, and more recently founded expertise--I wouldn't say expertise--but familiarity with molecular biology.

That pretty much defines my program in science, my aspirations in science. I want to discover and understand ways by which cells are regulated, focusing mostly now on cell growth and differentiation and more recently cell death. The way I designed the approach--Now, the tactical approach is to have each predoctoral or postdoctoral student tackle an independent project that belonged to the big scheme. I think that's where the payoff has come in the last year or so, that these things have started to make sense, that they are really components of one story. Most of the projects in the lab came with the general lipid question of signal transduction, asking the very basic, very naive question of the role of sphingolipids in signal transduction. By that time, it was becoming more obvious that phospholipids are involved in signal transduction beyond diacyiglycerol, beyond the PI cycle. People had started to make discoveries of other enzymes involved in signal transduction. Putting that with what had been known for a long time

about arachidonic acid, another lipid coming from phospholipids, the paradigm became well established, dogma now--to elevate it to the status of dogma--that phospholipids participate in signal transduction.

So what we wanted to do is ask the question about sphingolipids. Do sphingolipids participate in signal transduction processes? That has been one of the overriding concerns in the lab, the major program in the lab. There is another program on protein kinase C in the lab. I'll never let go of protein kinase C at this point. However, the questions became, again, more at the cellular level, at the biochemical level in the cell. It's sort of a funny niche. But what we've been after with protein kinase C is to try and ask questions and answer them in terms of how is this enzyme working in the cell at the molecular level in order to understand what function it serves.

Now, let me put that in some perspective, because I could almost make a statement now that so far we don't know what any one protein kinase does in the cell. We have a lot of correlative evidence. We have a lot of ideas. But if you come down to sort of very solid proof, you can almost not make any statements saying, "This protein kinase or this signaling molecule is really intimately responsible for that function." You almost cannot make that statement. It's sort of horrifying, knowing how much signal transduction studies have mushroomed over the last ten years.

So our approach has been, "Well, let's move the in vitro studies because that's not going to tell you about function. Let's move them to the cell, stick at the molecular level, and try to find out how one component really interacts with the other in the cell, and figuring out how this can result in changes in function." Now, I would say it's only now, in the sort of, what, fifth year of my work as an independent person, on the protein kinase C side, that we are getting some rewards from this approach, that we are starting--

HATHAWAY: You mean rewards along the lines of maybe getting some answers.

HANNUN: Of the big picture. Well, not even the big picture itself at this point. Of establishing some important and new connections with protein kinase C at the molecular level that we hope will direct us to function. It's going to be tedious, it's going to be long, but I think it's going to be building it step by step at the molecular level in the context of the cell.

HATHAWAY: I guess maybe what I would like to do is play devil's advocate a little bit, if I can, and actually maybe they will be a little more naive than devil's advocate kind of questions. They will just be "Duh?" kinds of questions.

HANNUN: Go ahead.

HATHAWAY: I get the sense that the biochemical approach that you use isn't just a matter of "Okay, that's what I learned and I'm good at that and so I'll stick with it," but that you think it's the best way to answer some of these functional questions, again, of cell biology and cells, not at a narrow level of genes and molecules and proteins and individual things like that, but the whole thing. I was wondering what your opinion was of perhaps more structural approaches or more straight genetic approaches. Are they just something that you see as obstructive or taking you down into narrower areas? Or is the competition doing it? I'm trying to get a sense of the wider context in which you're doing this, because you've been pretty steady with the biochemical—

HANNUN: Well, if that's the devil's advocate, we put ourselves through much more stringent questioning. Let me describe where I stand on things. I come from the clinical side on things. That always gives me a clinical perspective on things. It's very easy for me to see how something we do now, if it works out in a certain direction, can have clinical significance. I'm not saying it will. I'm just saying how I can evaluate every item very easily along those lines. On the other hand, I think my training with Bob Bell on almost, I would say, an esoteric subject of lipid biochemistry, and having I think succeeded in that, has given me a lot of self-confidence that I can learn new things at a very basic and molecular level. That's what I always tell my students they have to adopt as a policy: that tools are only tools. We're not a protein chemistry lab. We're not a biochemistry lab. We're after solving problems. think you articulated that yourself pretty well. We are after solving problems, irrespective of the tools. In the course of the last few years, we have come across all kinds of techniques.

HATHAWAY: I'm actually kind of being-- I'm still kind of thinking back in like '89 and '90, as opposed to-- You look through this [curriculum vitae] and there's a heck of a lot more, for instance, molecular genetics in the past, what, two, three years.

HANNUN: So we look at all these things as tools. If they help us to get to answering those questions, fine. Now, what are the questions? I think that's where they get imprinted with my philosophy and my bias. If I was a structural biochemist who was not only trained in X-ray crystallography but really loved the subject, I would pose questions related to X-ray crystallography.

HATHAWAY: What about collaboration? You obviously have enough familiarity with what goes on and why people ask structural questions and go at it from a structural point of view to perhaps at some point-- I mean, you must sit there occasionally and it crosses your mind, "Now, what if we thought about its spatial relationship to all that stuff?" I mean, what you can do, I mean, you can do functional studies that are--

HANNUN: But I mean that's where I think our lab may be a little unique. Maybe "unique" is

not the right word, but in a special group of labs, because we're not the very structural people like the people who do X-ray crystallography. On the sphingolipid side, I think before we started with the sphingosine story, believe me, it was 90 percent structural work with sphingolipids, all describing new structures and analyzing them.

HATHAWAY: And not going anywhere maybe or not going as far as you did with the--

HANNUN: Yeah. So I think the way I would like to think that we are special is that we do think of what we're doing at sort of the three-dimensional molecular level. That's always something I encourage in my students: Never work with a compound you don't have some visualization of what it looks like. Even your protein. Just try to have an arbitrary image of that, definitely your lipids. Have a good understanding of that structurally, and physical properties too. That's what obviously gives us an edge in studying lipids. But I think it's this ability to think about things on a molecular level and at the same time trying to push the whole system towards understanding very general biology questions of maybe more clinical relevance. Because if we did not have this—

And when I say "clinical relevance," it's not like I expect to have a drug in the next five years. I mean, it may be the next generation or may be never. But in terms of providing these kinds of novel connections that alert people, "Hey, these may be targets for drugs" or "These may allow us an understanding of diseases, pathology, physiology." This very global, generic clinical sense. A good sphingolipid chemist may just characterize the structure of the sphingolipid. A sphingolipid biochemist may want to understand how the enzyme works. You know, how does it take a sphingolipid and modify it and spit out a different sphingolipid and really become very sophisticated in that? I love that kind of science, but that's not what we're doing.

HATHAWAY: I would say that was part of what you were doing in preparation. For instance, the one article I really concentrated on, the '89 Science one [Y.A. Hannun and R.M. Bell, 1989. Functions of sphingolipids and sphingolipid breakdown products in cellular regulation. Science, 243:500-507], is almost partially a review article, right?

HANNUN: It is a review.

HATHAWAY: So clearly a lot of that work came out of your own experimental work, as well as your ability and your like-- You know, one of the things you like to do, which is to read widely. It's a piece of work about, I think, kind of all those incredibly subtle little "How does that enzyme work?" without maybe looking at-- And then putting it together.

HANNUN: So let me give you an example. I think we have discovered a couple of new enzymes in the lab. One is a sphingomyelinase. Now I will definitely go after-- We have already purified it. We're going to study it more, analyze it, understand the biochemistry of this enzyme. But I guess my overriding goal is we're not trying to understand the enzyme just to understand it, like maybe a sphingolipid biochemist would do, which is legitimate, which will provide new information and insight. We will still do that stuff--because we can do molecular and enzymologic studies--but always looking for hints about, if we understand how it works, how does that allow us to understand how the enzyme is regulated in the cell, and vice versa, so that we can place it in its physiologic context.

And the same thing we have developed much more--Because we have much better tools to study protein kinase C. Again, we now have-- For example, you mentioned structural. We are at a structural level with one of the isoenzymes. We have a domain of the enzyme that interacts with the actin cytoskeleton of the cell, with the matrix of the cell. So we've defined that interaction, because we were after a physiologic substrate for this enzyme at the molecular level. Now we've narrowed it down to like fifteen amino acids. But it's not because our idea was to take the enzyme and chop it up into domains and understand how each domain works in the test tube and stay there. We want to understand how it works in terms of can we pull out a physiologic real substrate for this enzyme so we can place it in its physiologic niche. So if you're putting together the jigsaw puzzle of the cell, you can take the piece of the puzzle and understand exactly how this piece is made up. We only do that in so far as we can know how to fit it.

So that's always been an overriding concern about what we do in the lab. I believe strongly that by understanding the structure of each jigsaw puzzle you will be able to fit it best. That's the duality I'm trying to explain in the lab, that while we are very molecular and structural, we do that so that we can place things where they fit. That may be too ambitious and presumptuous. So we understand or have a much better feel of how they could possibly fit. I mean, obviously, eucaryotic biology is so complicated. But to gain more insight into how these things fit in a global scheme. So it's this duality that I personally enjoy tremendously, going back and forth, saying, "Oh, did you do this structural study with ceramide?" which is a second messenger we think we discovered.

And ceramide, incidentally-- You take diacylglycerol from this picture [on the wall], put ceramide in, take phospholipids out, put sphingolipids in, you have almost an analogous situation. You take ceramide-- I mean, one of the questions we asked very early on was "What about the structure? What's unique to the structure?" And those kinds of studies led us to find that a very closely related molecule called dihydroceramide doesn't work. In fact, it almost does the opposite. So that gives us a much better sense of what ceramide does in the cell, because its cousin doesn't work.

HATHAWAY: It also maybe says something about the relationship of certain, you know--

HANNUN: Lipids to each other?

HATHAWAY: Yeah, And that they're doing opposite things, but they may have similar structures or parts.

HANNUN: Oh, absolutely. By doing sort of the mundane, which is taking ceramide and doing many compounds that look like ceramide and trying to understand how they work-- I shouldn't say mundane. It's sort of the rigorous biochemistry. You could have that for its own sake. A biochemist in a biochemistry department may be very happy just doing that for its own sake, and that would be considered a good contribution even by me.

HATHAWAY: So you'd fund that. Actually, you brought this up three or four times, so I'll jump in. And we'll get back to this ceramide. Your reasons why you've gone after it the way you have-- You would sit on a study section, fund something that was just going to-

HANNUN: Oh, yeah, I would. I mean, I think different people have different contributions to science. We wouldn't be sitting here discussing sphingolipids had people not spent a hundred years figuring out sphingolipid structure and biochemistry or, for that matter, all other cell-- I mean, the usual cliché, we all stand on the shoulders of people who stand on other giants' shoulders, that's very true. But I think I'm just--

HATHAWAY: Also the phrase has a wonderful history.

HANNUN: Maybe you'll tell me about that later.

HATHAWAY: Yeah. Off the tape.

HANNUN: I'm just trying to give you a perspective of what kind of science we pursue and for what reason. We are a very molecularly oriented lab, but we try to figure things in terms of biology. And we can work both ways. We can work the biochemistry or the molecular biology and move to the cell using that information, like finding out that dihydroceramide doesn't work, or, vice versa, try to understand something about the biology and then move back. See if that allows us to understand the molecule better or the molecular interactions better in vitro. Elaborate on that, move back to the cell, and see how things work at that level. It's a very dynamic interaction, but that's really what excites me about science. I think we've been quite lucky in both sides of the lab, the protein kinase C and the sphingolipid side. Definitely on the sphingolipid side we're sort of painting a very beautiful picture. On the protein kinase C, I think

we have developed sophisticated insight that we can now paint a more detailed-- Hopefully, I can start seeing a more detailed picture being painted because of that.

HATHAWAY: You prefaced a lot of this by saying you'd like to think your lab--its approach--is special and that there are not a lot of them doing it this way. Or maybe this, again, you used the word "dual," and I guess I used it too. So we're both using the word a lot and that's fine. I guess, one, I'd ask you who else is doing it. And it doesn't have to be-- Maybe you're aware of other people not even in related fields in the sense of they're not your competitors. They could be doing, I don't know, transcription, but they're doing it some way that's got this--I don't know what phrase I'd use--extra thing added onto it or something. That the goals aren't just what's produced from the lab and its papers but perhaps a more general understanding of biology beyond the areas you're working on. That's kind of a two-part question. Who else do you see--? Would you pattern yourself after somebody else? Do you see somebody patterning themselves after you? Is this something you talk about or verbalize with people?

HANNUN: I think I'm still too young and too junior to be patterned after. Who do I pattern myself after?

HATHAWAY: Or who do you talk to about these sorts of things, or has it all been saved up for me?

HANNUN: Yeah. Well, I talk to my wife about things. We collaborate. She's a physician-scientist too. I talk to myself quite a bit about these things. That's sort of, I guess-- I hope I have my creative moments. But beyond just creativity, I talk to myself quite a bit. I analyze strategy, tactics, individual days' results. At all levels I'm involved in that. I don't think I consciously have a role model that I pattern [myself] after.

HATHAWAY: I guess you started saying "unique," and then you kind of backed down from that and said "a few."

HANNUN: Yeah. I don't want to be presumptuous.

HATHAWAY: Well, but you're not naming any others.

HANNUN: Yeah, but it's primarily either because of ignorance or because of not wanting to spend ten minutes now going systematically over different areas or regions, saying, "These people do the same thing, these people don't." I mean, if you take a rundown of people doing

things around Duke, basic research, I think the more successful labs I can name have been mostly on the basic side of things, not really concentrating too much on the physiologic significance of those studies.

HATHAWAY: But on the kind of, like, as you said, the cellular or something--

HANNUN: I should take that back. If you now incorporate all the people who incorporate molecular genetics, I think these people are using the tools of molecular genetics to approach questions of physiology and biology. That's obvious. That opens up a whole group of people for you right there. I think we are a little different because we're not much into molecular genetics. We use it as an occasional tool, but maybe we're a little special because we're now using lipids in the same context and maybe enzymes. Was there another component to your question?

HATHAWAY: I thought the second part was really more, again, if you could find somebody to compare with and how the comparison worked, not just were there others and who were they. Again, I think, as you've just said, you talk to yourself a lot, so I think this is something maybe you've really given some thought to. It's not just coming off the top of your head as we talk. I mean, I'm asking you to drop names, because somebody can maybe read this and go and check out what you have to say even 150 years from now and say, "Oh, there is this kind of sense of doing things a certain way that may be communicated even here at Duke." You may have students, postdocs, who have gone on and they are struggling new PIs [principal investigators] and they've taken a lot of your methods as well as your--

HANNUN: Well, I think I'm still too junior. My students have hardly graduated, or a couple of them have only. We do discuss these issues, sort of the philosophy of the lab and the approaches to experimental design at all levels, the general, strategic-- In the lab, we actually once a year take off a whole day and go for sort of a retreat and discuss these issues. On a one-to-one basis, I usually meet with my students at home over dinner and discuss the general strategies and goals, rather than when I meet with them in the lab, which is on a day-to-day basis, and go over the daily results. Or even every couple of months they present their achievements and problems over that perspective. I still meet with them for more general levels of discussion. But I think we haven't advanced to a point where some of the students have gone on with those ideas. I don't know even how seriously they will take them after they go with them.

In terms of the other part of your question, we can drop a few names. Bob [Robert J.] Lefkowitz is considered the premier scientist, you know, the most known scientist at Duke now. He's a person who has been studying adrenergic receptors from day one until now, and he's done the whole thing with the biochemistry and the molecular biology, more biochemistry, more molecular biology. His work is superb. He has a large operation funded by the [Howard] Hughes [Medical Institute], internationally renowned as the premier scientist working with adrenergic receptors and probably as one of very few premier scientists working in receptors in general.

He's really in that group. You cannot mention signal transduction or receptors without talking about Bob Lefkowitz.

But I can definitely say that Bob Lefkowitz has never had in his lab--maybe in his subconscious or even long-term goals he has, but definitely not in his lab--a program to study the physiologic significance of these studies at the physiologic level. You can always say that if you understand how a drug binds to a receptor you understand how it works. That's plenty of justification for that great science for me. But he represents a group where he doesn't even want to invest in saying, "Well, do you make a transgene, let's say, with an adrenergic receptor and look at what happens to biology or knock out the receptor and see what happens? Or are the receptors important in cardiac failure, heart failure, or are they important directly in hypertension?" He's not looking at total-body or total-cell-system physiology. And the justification of his work-- I mean, he doesn't need justification. But he represents that class of science. I may represent more, now, come to think of it in that way, maybe of what the molecular geneticists-- In terms of using molecular biology techniques to answer questions of physiology and biology. Except we're not a molecular genetics lab.

HATHAWAY: You're talking about an outlook sort of.

HANNUN: Yes. The outlook may be much more similar. Now, unlike most molecular geneticists, who may be more involved with yeast or E. coil, we're involved with higher eucaryotic systems. This may be splitting hairs, too, because I'm sure many people who study enzymes or lipids want to know what they do to their cell system. I think our duality comes maybe more from in a way preimposing the physiology we're interested in, which is sort of leukemia growth and differentiation, on the biochemistry we're doing, rather than saying, "Well, we have this lipid. What does it do?" Do you know what I'm saying?

HATHAWAY: Right. You happen to come across this great sphingosine stuff. Nobody else did it. What does it do?

HANNUN: What does it do? Yeah. I mean, we have done some of those studies, not that we haven't, but it's never been the overriding concern of "Oh, if we find it does that, that's what we're going to be doing for the rest of our career." I don't know.

HATHAWAY: I think it's all very clear. You seem to be all of a sudden hesitating as you get--

HANNUN: I've never thought of it, I guess, in terms of how does it compare to other labs. I've always thought about what I want to do and how do the things we do stand up to what I want to do. That's my yardstick. It's not like "Am I closer to the Lefkowitz model or am I closer to the

[Michael] Brown and [Joseph] Goldstein or this and that?" I'm not thinking of it in that--

HATHAWAY: I guess I'm thinking more along the lines--actually, maybe I haven't approached the question right--that nobody is doing biology in a vacuum. And you read widely. Indeed, maybe I could have asked the same question about the four or five articles or the book you read, or, who knows, maybe it's a mathematician. Maybe before you pass on to other worlds you want to see some real serious inroads made with cancers and leukemia, where the basic science really pays off in a much more direct fashion and people aren't still doing retrospective studies about "Do we dose them at this level and this many times a day?" I don't know, that's I guess--

HANNUN: I think my perspective is to go after discovery of physiology at the molecular level. I think a lot of physiology has been discovered at the physiology level, at the whole-animal level, the whole-body level, at an organ level. But I believe a whole lot of physiology is still hidden in terms of the cellular level and subcellular level.

HATHAWAY: One would think of cancer being kind of the exemplar of how it has got to be hidden somewhere.

HANNUN: Cancer in a way is an opportunity to look at derangements in that physiology. On the other hand, it may be one of the very last things we can crack open as a scientific community because it's really a normal cell in disguise. We need to understand the normal cell function in great detail, I think, before we can understand individual cancers and how they go awry. I believe that there's a lot of discovery to be made in terms of even identifying new players, new lipids, or new functions for old lipids, new enzymes, new pathways. I think there are many pathways, the way elements in the cell connect to each other and communicate to each other. I think we know a few now: the map kinases and protein kinase C and calcium signaling and calmodulin kinases and transcription factors. We know a lot, but I think that's much less than half the story. I think that's a small fraction of what we're going to learn in the future. As I said, there's still many proteins and enzymes to discover, many DNA sequences, many lipids. But what's more important, we're going to become much more sophisticated in understanding how one component talks to the other. Only after we start building that element can we start dissecting out whole pathways in terms of taking something from A to Z. How does A talk to B to C to D to E? And it's going to be even more complicated because B can talk to C and C' (prime] and C' can receive a signal from B and B'.

HATHAWAY: And if it's got the day off, then F takes over.

HANNUN: Oh, yeah, absolutely. So it's going to be very complicated, but each one has to make their own contribution and slowly inch forward with that.

[END OF TAPE 5, SIDE 2]

[END OF INTERVIEW]

INTERVIEWEE: **Yusuf A. Hannun**

INTERVIEWER: **Neil D. Hathaway**

LOCATION: **Duke University Medical Center**
Durham, North Carolina

DATE: **2 April 1993**

HATHAWAY: I guess we decided that we'll pick up with a point you wanted to clarify.

HANNUN: Well, I think it's something we talked about yesterday in terms of how I view sort of the gestalt of the lab in terms of its soul. I had to think about it in terms of comparisons with others, because, as we talked about yesterday, I never really sit back and compare it to other models as much as how it matches up with what I want to do. But when I did think about it, the name that came up was that of Jim [James E.] Rothman, who studies vesicle transport at the very biochemical level. I find that fascinating because it's nothing very intimately related to what we do at all. But I think the approach [is similar] in that there's a fundamental problem of biology--trying to understand how proteins and lipids get moved along in the cell and sorted to different places in the cell--and the approach has been molecular and biochemical, not genetic. I find that a very gratifying approach because it identifies the components of the system but through functional studies. It identifies simultaneously, I guess, the function and the component because that's the approach.

HATHAWAY: Instead of this kind of perhaps a two-step or a process where you identify, clone it, and say, "Okay, here it is," and then move on to the next thing and let somebody else mess around with it.

HANNUN: Exactly. The classical biochemistry or genetic approach is you have something and you try to figure out how it works or what it does. You have an enzyme and all you're interested in is how this enzyme is regulated. Or you have a clone, and you want to know what is the function of that clone. That's a major, I would say, problem in the reverse genetic approach, where you really take a problem of fundamental biology and you pick up components of that problem but often you don't know what those components do. You don't have the functional significance.

HATHAWAY: And you may not even care, right?

HANNUN: For a while you may not care, as long as you're cataloging and assembling the pieces, but sooner or later you need to see how they fit together. You have to move to that next level of functional studies.

HATHAWAY: Do you think that's harder work?

HANNUN: What, the biochemical approach?

HATHAWAY: Or the fact that once you get past the catalog you might as well do something with the things now that you've identified. Is it harder to then do the functional?

HANNUN: It is harder. It's probably getting easier with time as people understand structural motifs in terms of functional consequences. From sequencing genes one could always glean some idea about how things work, and with more insight and cleverness and whatnot you could-- I would think that an important goal for most molecular geneticists once they've identified something on a pathway is to find out how it fits in that pathway and how it works at the biochemical level, although many molecular geneticists are not trained in biochemistry, so it may be very difficult to move on to that level. Just as many, I guess, biochemists are not trained in molecular genetics, so they can't bridge that gap from the other direction, either. I think that's where the functional approach is best--again, I hate to use that terminology--best exemplified by this example with Jim Rothman. That's appealing to me.

HATHAWAY: And as you say, it's not anything to do with-- It's not a matter of comparing content, it's a matter of comparing approach. And even perhaps on an ideological level, [it shows] why one would be interested in biology and what one wants to get out of investigating. Where is he [Rothman]?

HANNUN: He has moved a few times. He is now at Sloan Kettering [Cancer Research Center]. He is head of a department or something at Sloan Kettering.

HATHAWAY: I know I've talked about him with somebody before-- Isn't that awful? I believe it was Greg [Gregory S.] Payne.

HANNUN: There are other people who follow a similar approach. Gunther Blobel does related things in terms of nuclear structure and function import. There are major labs that follow that paradigm. That's the kind of approach that I find appealing.

HATHAWAY: Actually, there's somebody else I've talked to about Blobel. And again, to talk about his approach, if you wanted to say a little bit-- Maybe it's again just something you're aware of. You see his name or his lab's work in a journal and you read it just--

HANNUN: I mean, Blobel may have started with things more from the biology part and been more recently moving into the molecular aspect of it. But I just needed the whole thing just as a clarification.

HATHAWAY: Sure. I was listening to the tape last night. I didn't want you to think that-- Actually, that's something I should have made a note of to make sure I definitely got on tape. I was not talking about like some sort of role model hero or "Who is this person, and I'm imitating him," but more along--

HANNUN: Yeah, because I think that does identify one approach to science. There are a few scientists that probably conduct science with this approach, although the majority have probably a more basic approach.

HATHAWAY: I think it's also kind of an important question to ask from my point of view because I think there are issues about whether it doesn't matter who is doing the science and when. "There's this truth to be found and we'll find it," versus a much more, I don't want to use the word "relativistic," but a much more subjective understanding of how science gets done. Which is that the style and the personalities and the people actually affect content, not just as some sort of side effect, but that people's values and approaches and mores affect the kinds of questions they ask and how they go about finding the answers. To have people talk about that on tape, these sorts of things, is, I think, worth spending some time on, not that I have a position that I hold on who's right and wrong, but those are the kind of extreme ends of the issue. So that's what I was really getting--

HANNUN: Yeah. Well, that again sort of also is a more philosophical question. And I want to borrow again from William Harvey, the mathematician. It's sort of a mathematician's apology-- why engage in the game of mathematics and still consider yourself a functional member of society. I have to justify my work, too, from that point of view.

HATHAWAY: To yourself.

HANNUN: To myself, yes, not to NIH [National Institutes of Health] or anyone else. Why

engage in the abstractions of basic research and spend my life doing that rather than either work in the clinic, in academia, or for that matter go and immunize children in Bangladesh or some Third World country. It's a serious philosophical question.

HATHAWAY: You think one especially that confronts or is a part of being a doctor, I mean, of being in--?

HANNUN: Yes. Because I do have that other hat and that capacity to do that. These are real life possibilities and options. Almost instantaneously-- I mean, I could switch--I do switch--a couple of months a year from one to the other. I could switch permanently. So I have to justify my role to myself very carefully. But the philosophy of it beyond that-- I mean, that's a very complex issue in terms of, yes, we can say I can work with one patient at a time and maybe provide a little increment in the well-being of that patient or work in science and try to enhance knowledge and that may touch on human health later on. I don't think that argument stacks up real well in favor of research.

HATHAWAY: Really?

HANNUN: I don't think so.

HATHAWAY: I think it's a common one that's, again, without any kind of serious studying on my part-

HANNUN: A common denial.

HATHAWAY: Or a common--

HANNUN: Conclusion?

HATHAWAY: Yeah. Or "Yes. I'm doing basic research. I'm an M.D. But I think that I actually am contributing something more basic and in the long term helpful to more people." And, again, I'm not thinking of anybody in particular. I haven't read any studies. I just-

HANNUN: Yeah. I don't have data on that at all. I'm sure many other physician-scientists believe that they may be more useful as scientists, although I'm pretty sure that many other

physician-scientists are more stuck in science because they got to be disillusioned with clinical medicine. See, I don't have that problem. That's why I really have a true option here. I don't have a problem with clinical medicine. I enjoy it tremendously, and I'm very effective there. I establish good rapport with patients, and that is half the problem right there in helping patients out. So I do have that dilemma. I think my role may be more in-- In a way, I have a deep-rooted belief that excellence and driving knowledge per se, in a very abstract form, is extremely important. I think people who can provide role models, who can train younger people along the same lines, almost like Aristotle or Plato-- If you can touch a few people and carry a tradition of striving to be as analytical and as innovative and as a contributor to new knowledge or new ways to understand existing knowledge--which is, again, new knowledge--it is very important. I really look at it in almost a political sense rather than a philosophical sense, that if we can move human society one notch further across the board in the striving to excellence and to more intellectual aspirations, I think that's a tremendous benefit to mankind. I look at it from that point of view.

I really don't believe that what we're doing with leukemia cells is really going to contribute to leukemia therapy in a very real sense. It may. I hope that someday it will offer a lot of knowledge about that, but I can't sort of stick my neck out for that, because if it doesn't pan out--and most examples in science don't pan out in terms of resulting in concrete health benefits--I would be a very frustrated and vulnerable person. No. think of it more in terms of I'm contributing to how people understand things. I'm contributing to how younger students develop their intellectual skills in research. That probably will touch them beyond that, you know, beyond the immediate results of experimental biomedical research. And if that is part of a bigger tradition that maintains that, I think the impact can be tremendous.

HATHAWAY: And you mean in a sense of them passing it on or having x number of people with a sense of what education and investigation and abstraction and analysis and human kind of endeavor is?

HANNUN: Yeah. In terms of myself being part of a much bigger group of people doing the same thing or at least achieving similar results and myself grooming younger people directly to do that. Some of the most rewarding feedback I've had-- People who teach lipid biochemistry come and tell me, "Hey, we teach your papers in our courses on lipid biochemistry."

HATHAWAY: Maybe there's a textbook in the future if you're getting this kind of feedback. No. I'm being serious.

HANNUN: It's that kind of reward that I appreciate a lot, and also having younger people think about science in a different way. My bias is that it's a more enlightened way, a more productive way. If you can carry that across the board and improve everyone's ability to analytically look at things and synthesize information--and they do it across the board in all their social functions--I

think society will be much healthier. I'm not only talking about the U.S. society but the world society at large.

HATHAWAY: Do you see this as something that you learned from--? Well, you wanted to say something. Let me let you finish your thought.

HANNUN: Well, coming back to the original question, I didn't go on a tangent here not to come back to the original point, which is that [that] is my dilemma. And since it is my dilemma, I'm always trying to make sure that what I'm doing in science is unique, that if I'm not in science there would be a gap, maybe a very, very tiny, small gap, but there would be a gap because other people won't be doing what I'm doing. And it's something I also transmit to my students, because there is always this "scooped" idea running around in science, "We got scooped" or "We're going to get scooped" or "Someone's going to beat us to the punch." I always tell my students, "That's not what you're going to get in my lab." I try to make sure that they understand that because, one, we're trying to solve a problem. If anyone else contributes to solving that problem, that's only going to help us. Again, it has practical benefits, too, because if other people start working on our problems, our problems become more important. That's a definition of being important. And it helps us really look at things with other-- I mean, no one's going to do the same thing we're doing exactly verbatim. They're going to either use a different cell line or a different agent or a different thing. So we're going to learn more. In the long run, that's going to make our story even more solid. I always try to transmit that to students. To me, that's important, that almost avoiding trying to solve problems that would put you in a position of being scooped, because that automatically implies there are other people working on that problem. If they're capable, competent people, I feel redundant. That's been a major steering force for me in conducting research.

HATHAWAY: Is it also maybe a reaction to your sense that there's a lot of that going on or too much of it?

HANNUN: There's a lot of science going on, absolutely.

HATHAWAY: That's just strictly-- I mean, "Oh, they're doing that. That looks good. Let's try it ourselves"? Or is it just that you think, "Well, okay, all of a sudden--"? I'm trying to think of a-- Let's talk about gene knockouts, just because I keep running into it, you know, where literally in some cases there's a race who is going to get--

HANNUN: The knockout first.

HATHAWAY: First. And let's say that there are, I guess, fifty so far, there have been fifty.

HANNUN: I don't know how many genes have been knocked out.

HATHAWAY: The first two that were done were the same. And that was apparently like--this is hearsay from my point of view because I have not read it or seen it, you know, that kind of direct way--but that these two labs were-- I mean, it wasn't a matter of "Oh, they're doing it. We're going to do this one too." They both came to the conclusion "This is a good gene to do it on for these different reasons," and boom--

HANNUN: Well, I mean, again, we always find ourselves in that kind of situation, but it wouldn't bother me.

HATHAWAY: You'd still go on with the work or--

HANNUN: If that gene knockout is part of a general question about understanding how something works in a system, that's fine. You do it even if you get scooped on that. That only helps you move faster and further and makes you think how you can contribute more to that and deeper. But with me it goes even at the level of choosing the projects in the lab. Definitely every student in my lab gets what I think is a new project, you know, something that hasn't been done somewhere else and that is unlikely that it is being done by someone else. But equally important is to make sure that it fits in a scheme where the whole scheme is a novel angle of things or a novel contribution.

Maybe now is a good time to discuss how the lab is structured. I don't know if you-- But to sum that part up, therefore, in terms of the philosophy, I want to make sure that what I'm doing in the lab is not redundant. That's important justifying my existence in the lab. Because if I was in a race in a knockout experiment--that means there's someone else knocking out that gene--it means that if I went back to the clinic I'm going to be contributing something important, while if I'm in the lab I'm going to be contributing something redundant. You could carry the same argument to the clinic and say, "How do you contribute something unique in the clinic?" My gut feeling is there is always opportunity to contribute something unique and different in the clinic. Maybe if you're in a tertiary referral center like Duke [University Medical Center] or Harvard [University] or something, there are many other competent people, but then there is really a lack of superspecialized people definitely in the world at large but also in many areas of this country. And even in that context I could contribute new things because I've been through that, I know. I mean, I can't kid myself and say, "I cannot contribute."

So that's an overriding force here. How has that helped structure my lab? I think that's a major steering force or guiding force in structuring the lab. Maybe my own excitement about

some biology problems has dictated the themes we want to address. But trying to do something that establishes a unique, I would say, niche for us, at the approach level, as well as at the knowledge level, has dictated the structure of the lab.

The two things that we do in the lab, if I can spend just a couple of minutes on that-- We have two programs, one on protein kinase C and one on sphingolipids. This is a major burden to me because these are two different disciplines now. It's at the point where I'm exhausted, basically, in trying to keep up with those two areas, run two programs independently, almost independently. Yet I'm still not willing to give up one or the other. Both have turned out to be very rewarding. My initial bias that they're good for the health of each other has panned out. Let me explain that.

The sphingolipid story is the easier to explain. It started--I think we also talked about that--when we found that sphingosine inhibited protein kinase C. We asked-- we talked about that--"Do sphingolipids offer signaling molecules?" And that's the story we have built. The answer seems to be yes in at least one, probably two, situations. In the first situation, which is really the better developed story at this point, which we have been working on for four years or so, we have found that a number of extracellular hormones and agents turn on what we call the sphingomyelin cycle of cell regulation, as we've termed it, in analogy with the PI cycle. This has resulted for us in identifying either new entities or new functions for old entities. We have a new enzyme, a sphingomyelinase. We have a new function for sphingomyelin now as a relay or a switch, and we have ceramide as the messenger from that relay switch, generated as a second messenger. We believe, at this point, ceramide functions at least in part by activating a protein phosphatase.

What's been tantalizing for us over the last few months is that we're now getting an appreciation that this pathway of cell regulation seems to be much more involved in negative regulation of cell growth. It's an antiproliferative pathway. From our very recent studies, we believe it's important in inducing programmed cell death. Why is that important? One, it's important for all the biology and all the implications of the biology. That now we may have new tools and handles on mechanisms that counter proliferative signals, that make cells slow down, that may even instruct cells to die if they should die. This is of fundamental importance in biology. It's of great importance in cancer. The way we think of it is those instructions served by the sphingolipids are important to allow cells to adjust to hazardous situations. If a cell gets beaten up because it has suffered hypoxia, ischemia, lack of oxygen, or some other stress or some other injury, you don't want that cell to go on and divide with all the injury because you get a mutated cell, and that's sort of inviting abnormal function, even cancer. So these are the molecules that instruct the cells to "Slow down. There is injury in the environment or injury in the cell. Maybe it's time to start repairing that injury."

HATHAWAY: And this you think is just an intracellular kind of thing or do you think is some sort of whole biological--?

HANNUN: Well, I think at both levels. It operates definitely in response in cell-to-cell communication, or environment-to-cell instruction, but it probably is going to emerge that it also operates as a sensor inside the cell.

HATHAWAY: Kind of a federalist system, if you will, with the federal government and the local government kind of working it out together.

HANNUN: Pretty much, I think. The instructions can come either from within or from without to slow the cell so that it can size up the damage, or maybe even some of the sphingolipids are the molecules that size up the damage. And if the damage is irreparable, the cell is instructed to die. If the damage is repairable, then the cell is instructed to start repair. Once it's healthy again, those signals may fade away, or those sensors, and the cell—

HATHAWAY: And you think it's the sphingomyelin cycle that's doing all those levels. In other words, it's the monitor and the messenger.

HANNUN: The sphingomyelinase part and the sphingomyelin are sort of the sensing part of it, and ceramide is the second messenger, the signal that goes on to instruct the cell exactly.

HATHAWAY: One of the, I guess, more recent articles--and I wish I could just pull it right out: maybe it's the one that is just two weeks old--[seemed to say that] though it seems to be competing with the phorbol ester protein kinase C--

HANNUN: Pathway.

HATHAWAY: Right, that it's not the only thing out there but-- Am I making the picture too complex too quickly?

HANNUN: No. That was my other point where I think this is significant. One was the biology. The other is "Where does this pathway fit in terms of other pathways?" The way now I'm trying to explain it and think about it is a major drive in cancer biology over the last twenty years has been understanding what makes cells grow, and the knowledge base there is phenomenal. We have discovered--scientists have discovered--dozens of players in those mitogenic pathways: the signals that drive cells to grow, all kinds of mitogenic hormones, stimuli, receptors, second messengers, protein kinases, transcription factors. The list is really extensive. And the oncogenes that have come in to fit with that have really solidified that structural conceptualization of mitogenesis.

And that's something I tell students. If I tell you that hormone x works on the cell to induce it to turn from red to blue and I ask you, "How does it do that?" in terms of all the signaling and all that it turns on in the cell, the way to answer that is actually very simple. My next question would be "Does hormone x in any cell system instruct the cells to divide or not?" Now, it may be that hormone x, like thrombin in human platelets, makes platelets aggregate. Yet in endothelial cells it may make them divide. Once you make that connection, you can bring in all that we know about the mitogenic pathways and understand how thrombin works. You can relate it to tyrosine kinases, diacylglycerol, calcium, protein kinase C, the whole concept. Now, platelets don't have a nucleus, but in other cells thrombin will do a lot of those things. Your yield from investigating those pathways with thrombin is going to be phenomenonally high, and the understanding you're going to develop is going to be incredible. Now, if I tell you hormone y turns the cell from red to green, and you answer my other question that "Well, no, hormone, y doesn't make cells grow. In fact, in some cells, if it does anything, it makes those cells stop growing," I can't give you anything as a structural framework to understand how hormone y works.

HATHAWAY: I think just yesterday, going through the [James D.] Watson-[Nancy H.) Hopkins book [Microbiology of the Gene]-- It's way out of date of course, but it gives credit to someone. I think it's actually in transcription, but in the regulation of that there's something that actually turns things off. In other words, it tends to work as a negative-- This is like the only example, and this is, what, '86, '87? "Oh, isn't that novel?"

HANNUN: So basically there is a paucity in understanding how a signal that turns off a cell works. That to me means there's a whole missing black box of what's happening inside the cell. Again, for the record, I must state that hormones x and y do not necessarily [have] to be primarily a promitogenic or an antiproliferative hormone--

HATHAWAY: You even mentioned that maybe hormone x could be the negative regulator and another--

HANNUN: Another cell type, that's possible. But as long as you're trying to match up-- So even many of the elements in the mitogenic pathway, what I'm trying to say is they were discovered because they are involved in mitogenic pathways primarily, or a lot of the excitement about them has come because they are either oncogenes or regulators of oncogenes or substrates for oncogenes, all related to the mitogenic pathway, although they may carry out other functions. For example, thrombin can stimulate mitogenesis but turns on platelets. Protein kinase C can activate platelets but can induce cell proliferation. So there are a lot of different functions for even the same molecules. But the thing is, if you want to understand how a molecule y that turns off a cell works, there is really, a tabula rasa, a very blank page there.

HATHAWAY: Can I interrupt?

HANNUN: Sure.

HATHAWAY: Why? Do you know why people would have just missed the point?

HANNUN: A couple of good reasons. I think one is that even at the biology level-- Because a lot of this work has really been driven initially by biology. Although now we're at a stage of molecular biology and biochemistry, a lot of the discovery was initiated at the biology level. You culture cells, take what's in the soup, find a growth factor there, and then purify-- So the biologists always turned away from things that inhibited growth.

HATHAWAY: Just because of what they had at their disposal, which are these things that they need to plate and get them and get them to grow.

HANNUN: There has always been great skepticism about things that inhibit growth. Why, I don't know.

HATHAWAY: A kind of mental block or mental construct is there maybe about evolution or--

HANNUN: I've heard it from many biologists who work with growth factors.

HATHAWAY: Just the name, I mean just the language and the semantics or whatever.

HANNUN: Whenever they came across an activity that inhibits growth, they would pursue the activity that promoted growth. There was skepticism, and skepticism generates more skepticism. Basically, things that inhibit growth were looked down upon in terms of—

HATHAWAY: And must be tougher to investigate. Something that's going to turn off your system is going to be a real pain in the neck, isn't it?

HANNUN: It is. I think that's part of the skepticism. It's very difficult to investigate. I really haven't explored the roots of that. Definitely those things were there before I even started in

science. So I definitely was aware of skepticism about all those things back in the early eighties, even the concept that some of those hormones were called chalones, almost in a pejorative sense that if you talk about a chalone it means you don't know what you're talking about. So I think part of it, yes, is the complexity of understanding the system, because it turns out that many of these things that inhibit growth actually sometimes induce cell death. Now, that has been a no-no for cell biologists. Things that induce cell death are not real.

HATHAWAY: It's like suicide.

HANNUN: Well, now we understand it as cell suicide, but back then I think cell death meant you're not growing the cells right or you're doing something wrong,, you can't get information. Now two breakthroughs have come that have really sort of started rectifying the imbalance there. One is a conceptualization of necrosis as a form of the cell death that really happens when you put a flame to a cell and burn it. And apoptosis, which actually was formulated in the early seventies but it's only picked up very recently, again, because an oncogene was found to work by inhibiting apoptosis. Again, you needed sort of that kind of connection, the oncogene first, to understand, "Oh, this is inhibiting cell death, so cell death is for real now." And now, whenever I explain cell death, you know, this apoptosis to someone, even an undergraduate, it's so intuitive that cells and the body need that kind of machinery to make sure that when cells need to die they go ahead and die and don't injure the body in the process of dying. So that was a brilliant formulation, I think, that there is programmed cell death, one, two more pathways, I don't know. There's at least one biochemical molecular pathway that instructs the cell to go ahead and die. So that's a brilliant breakthrough.

HATHAWAY: There are actually quite a few Pew scholars now--

HANNUN: Working--

HATHAWAY: Oh, yeah. They're coming into their own. There were quite a few talks--

HANNUN: I didn't know that. But it's picking up.

HATHAWAY: It's a hot area.

HANNUN: It's _a hot area, absolutely.

HATHAWAY: Could you attribute the change--? I mean, to whom could you--? Isn't it a situation where you need to be so-and-so, the PI [principal investigator] in the lab, but just maybe to--?

HANNUN: [A. H.] Wyllie and [J. F. R.] Kerr in 1970, I think, published the first paper at the pathologic level distinguishing two kinds of pathology, cell death by necrosis and cell death by apoptosis. But I really think there's been a lot of work on-- I should actually say two things. One is this connection to bcl-2, which is an oncogene that works by inhibiting cell death. The other is showing that this mechanism of cell death is associated with DNA fragmentation in a very orderly fashion. That I think sold the people to "Hey, we can reduce the cell death to a biochemical measure." I think that has been a very important-- And I really don't know who is the first group to show that.

HATHAWAY: You've certainly given the future readers of this plenty to go on. That's their job, not ours.

HANNUN: The other major breakthrough in legitimizing mechanisms of growth inhibition came with the study of, again, cancer. One was the p53 oncogene, which initially was thought to be an oncogene, and I think the consensus now is it's an anti-oncogene. You can mutate it to become an oncogene, but its function in the cell is to stop growth. And the other is definitely the retinoblastoma gene [RB] product. RB now also causes cancer by not being there, by being eliminated functionally. And, again, the formulation for that started in 1970 with an epidemiologist-pediatrician [Alfred Knudson] going through the disease and how it's expressed, saying, "Hey, this looks like two alleles have been knocked out." It looks like a recessive disease at the molecular level, although you look at the pedigrees and you say this is an autosomal dominant [condition]. With the cloning it was verified immediately that this is a gene that's missing in those diseases. It's missing, and it results in cancer because it in a very sort of general way inhibits growth. So I think those two formulations came in to show that "Hey, there are real molecules working to suppress growth, and the mechanisms of cell growth inhibition and death are real biochemical molecular mechanisms."

Now, why is that important for us? Because I think that's where sphingolipids currently look like they fit in. They may provide us with some of those tools that we had in the seventies and eighties about understanding mitogenic pathways. These may be equivalent tools in understanding all the antimitogenic pathways. This may also be the reason they were not discovered until now: that they operate primarily when cells are instructed to slow down or to die, and people have been avoiding all that area of biology.

HATHAWAY: I'm also trying now in my mind to recall what the situation was then. You're working between the two labs. In other words, what are almost the accidents that allow and even--? You weren't even sure in 1987, '88, '89, about-- Oh, this is all, you know-- Down

regulation is not the right word, but—

HANNUN: Oh, the biology.

HATHAWAY: Right. That would have allowed you to see this come out as well as--

HANNUN: In retrospect everything seemed like it was laid out magically.

HATHAWAY: Just to be found.

HANNUN: Just to be found. But obviously it's more our limitations in thinking that have actually delayed us.

HATHAWAY: Oh, I would agree with you.

HANNUN: It's funny. In this context, maybe we should mention the Pew [Scholars Program in the Biomedical Sciences], because when I wrote the Pew [application] it was actually the first month I was setting up my lab. That's when I wrote the Pew proposal, incidentally the month my triplets were born. I remember that distinctly. The proposal was aimed at that global thing in terms of "Hey, let's look at sphingolipid products that can be second messengers." In retrospect, I think it took quite some trust in my abilities to fund me. But I think that's also maybe the tradition of the Pew, that they weren't really looking like NIH does in terms of "Oh, is this well and proven and not necessarily wise but a safe investment?" And the Pew I don't think considered that at all, because if they wanted a safe investment mine would have been the first out the window. There was definitely a lipid person on the committee there. I think it took some insight and trust that lipids are important and this guy may be qualified to look at the sphingolipids.

[END OF TAPE 6, SIDE 1]

HATHAWAY: Since you were bringing up the Pew and the situation there, as well as since the copy of the NIH grant application you gave me is dated from around this same time-- I'm not going to play devil's advocate because in a sense the reviewers already have. There seems to be a question about, "Oh, God, here comes another thing about protein kinase C" and "Isn't this stuff everywhere?" and "It reacts with everything" and "Is this going to work?" There seems to be this issue--and I think you kind of brought it up--that even with you there was-- You know,

you saw that this could really pay off, not "make you a famous person" pay off, but answering some basic questions about biology.

HANNUN: Well, actually, you touched at it in a very sort of specific way in terms of PKC [protein kinase C] because that was our initial connection to sphingolipids, but in my mind I never thought of sphingolipids as peculiarly associated with PKC. I thought of that as a lead into starting to examine sphingolipids. And again, to size up the Pew evaluation, I think that came as a wonderful boost of morale that you could still do innovative research and carve a new area and attack a new area.

HATHAWAY: And I think where the NIH is saying, "Okay, slow down," there's some mention of "You don't have this incredibly detailed thing of what you're going to be doing every minute for the next five years, because this is already risky." And somebody said, "This is somebody who is just starting out, and don't they--" It's almost like they're suggesting you're arrogant. Whereas I think the reaction among people of the Pew is "Boy, this is what we're after some of the time, and this is where we're going to see what-- This is where we throw some money at it and don't worry about it."

HANNUN: That, again, maybe we can come back to that, but I think this is how science should be funded, to encourage excellence and innovation and not the immediate results. But that maybe we can come back to--the qualities of science.

HATHAWAY: It's certainly a major issue, even if Bernadine [Healy] is no longer there [as head of the National Institutes of Health].

HANNUN: Oh, yeah. It's still a major issue. And the Pew money had practical effects that went beyond the money. One was the meetings. The annual meetings were always mind-boggling because it showed me that I wasn't alone. There were nineteen people in my year and sixty other people. Each was embarking on a new story, with new approaches, new ideas, and a lot of it was way out in left field for me in terms of a lot of biology, even some botany. But it showed me that if you sit back and think, "Hey, how can we be innovative here?" you can be. And there's a lot to be innovative about. That has been very helpful to me because, if I wanted to be innovative on my own and went through just the regular NTH channels and whatnot, with the years it's becoming more and more coercing in terms of not being innovative. The Pew is like a breath of fresh air. My idioms are terrible, so you must correct me. Actually, they've gotten me in trouble many times, just misplacing an "off" into an "of," and people can get irritated.

HATHAWAY: I've found that very articulate people, when English isn't their-- They actually are doing wonderful things with the language, and I actually enjoy them.

HANNUN: I do commit a lot of errors in either idioms or whatever. So the Pew was really fascinating from those aspects. It was also important practically because I think my chairman, Joe [Joseph C.] Greenfield [Jr.], head of [the Department of] Medicine at Duke, who was very supportive from day one-- He trusted me more at the sort of a gut-level feeling from knowing about what I did and how people who were very close to me like Bob [Robert M.] Bell and Jim [James E.] Neidel viewed my work and abilities, rather than from the point of view of saying, "Hey, he solved this problem this way, so he is good" or from the point of "Well, we really need someone doing this kind of work in our department." So with that kind of trust, getting--

HATHAWAY: It was a personal thing. I mean, even if he wasn't personally close to you, what it was you could have been doing, you know, God knows what.

HANNUN: He wasn't close to my science either. So it was very good to have this kind of outside consolidation of his trust, his belief that--

HATHAWAY: When you've got somebody on your side kind of taking the plunge with you or whatever--

HANNUN: Well, it's a vote of confidence from the Pew that "This guy was chosen among a very competitive group by a very prestigious group, so what I thought about him must have been good." That was helpful. These kinds of attitudes and support are very essential to survive. So that's where the Pew came in. A year later--or a couple of years later--I got an American Heart [Association] Established Investigator [Award]. That was another vote-- I mean, that definitely wasn't important for the dollars, again, as much as the vote of confidence to get from the outside peers--

HATHAWAY: And this one now, I'm almost afraid to pronounce it.

HANNUN: Mallinckrodt [scholar).

HATHAWAY: Mallinckrodt. Yeah. That was really something. That's one person. Is that bucks too?

HANNUN: Oh, yeah.

HATHAWAY: Yeah. That's money, too, that's great.

HANNUN: Yeah. And that's one person a year chosen.

HATHAWAY: Oh, really. Do you mind--? We can spend a couple of minutes-- I mean, since we're talking about funding or how these day-to-day and practical aspects of survival affect doing science, did they just call you up and say, "You win" or--?

HANNUN: No. They invite a nominee from several institutions, one nominee per institution from several institutions. They ask them to submit--

HATHAWAY: Is it the same institutions every year? Or they just pick--?

HANNUN: I think different institutions, different years. There may be a few that sort of-- Like the Pew does. It's not as extensive. The pool is not anywhere as extensive.

HATHAWAY: The Pew's criterion is $17,000,000 in NIH funding at an institution. If there's twice that or there's the medical center plus the-- Then they're allowed two people to apply.

HANNUN: I really don't know the mechanics of the Mallinckrodt. But they invite several, and then they have five who go to Saint Louis for personal interviews with a group of lay people--a lawyer, a businessman, a radiologist, I think, but really no basic scientists.

HATHAWAY: And who is funding this?

HANNUN: The Mallinckrodt Foundation, which is a foundation based on, I think, the Mallinckrodt Chemical Works.

HATHAWAY: And that's anything to do with biomedicals.

HANNUN: Yeah. Chemical reagents and biomedical supplies. It was fascinating because I had to describe my research and interact with these people--four or five different people--over an hour, describing my work in very simple-- Not necessarily simple, but be able to articulate it--

HATHAWAY: Like you're doing here.

HANNUN: Well, no. You've read some of my work. You've met other scientists. Those are people who haven't done science, haven't read science either. So it was really an experience. I prepared for that a little bit, a few hours, mostly with my wife [Lina Obeid Hannun], in terms of how can I come across to those [people]. And I think I did. We had a very lively discussion.

HATHAWAY: I don't know if your wife would have been the best-- I mean, as a confidant she would have been, but as somebody--

HANNUN: Because I was starting out from a very technical-- You know, where you could easily lose the people, lose the forest because of the trees. But I think starting at sort of a common ground, finding the common ground, we ended up with a very lively discussion about the science. It was really intriguing. So one can be effective in communicating excitement about science to the lay audience if you can discover the common ground. Again, that was another vote of confidence. My experience with NIH has been much less of-- The review process at NIH is very rigorous, but it's becoming more exacting and playing it very, very safe, and that's at the sacrifice of any leeway in innovativeness. You can't go in with a grant, say, "Hey, I'm interested in that. I want to look at how--" You have to lay it out in almost excruciating detail in terms of-- I don't know if we're going to come back to that later or now is the time for this.

HATHAWAY: There's a few more things about your research—

HANNUN: Because we took off from how we built our research.

HATHAWAY: It's actually amazingly coherent, and will be, I think. Don't worry. Let's continue with the NIH since it's--

HANNUN: Well, biomedical research is in a big mess now, and it's in jeopardy, Because the way I see it, the scaffold, backbone, to biomedical research in this nation is the RO1 given out by NIH, the individual research proposal. That's the one that's been taking a beating year after year, for a number of reasons. First, the research budget has grown--the government, the NIH, has grown--but at a slow pace. And number two, the government is mandating more and more how a lot of that research money is being spent. That is being subject to a lot of lobbying groups. I think the AIDS lobby has been very effective in pouring in a lot of money into AIDS research, which is fine. If you want to make progress on a specific disease, you need to fund

until saturation, so that you fund a lot of garbage, but you never know when the real insight comes from what lab doing what at what time. So that's fine. But it has also opened up the eyes of many other groups that say, "Hey, breast cancer. We want to fund breast cancer [research]."

HATHAWAY: There's a very interesting article or series of pieces in Science recently, too, about that, and the woman talks quite openly about tactics.

HANNUN: Yeah. People are starting to talk about tactics and lobbying efforts, which is fine, but the way I would like to see it is that if those moneys come in on top of what's in the potty--

HATHAWAY: The pot!

HANNUN: The pot. Too many children! Geez, what a goof! But it's not happening that way. So what's giving is the R01. My prediction is there's going to be more and more of people with prostrate cancer. The older men are going to lobby for prostrate cancer research.

HATHAWAY: They may not have to lobby. The Senate might be full of them, themselves, right, and they just-

HANNUN: Any group that can get an audience with the Senate is going to make an effective case.

HATHAWAY: What about the--?

HANNUN: Let me sort of finish that train of thought. So that's one problem. A lot of money is now being mandated. You know, cancer centers. We have a cancer center here that gets a budget of $2.5 million a year, and there are dozens of those. You know, $2.5 million a year, that's fifteen to twenty-five R01's. That's a lot. And that money doesn't filter much into research. That does not filter into basic research. It filters into other health issues but not directly into basic research. So there is that problem.

Another major problem is, unlike medical schools that have regulated entry into medical education, graduate schools in biomedical research have not regulated entry, either at the level of graduate admissions or at the level of junior faculty, so there is a tremendous surplus now that does not match the demand.

HATHAWAY: And that's relatively new, isn't it? I mean, it's really like there was such expansion in the field until what, God, even the end of the seventies, early eighties.

HANNUN: There is expansion going on right now.

HATHAWAY: I also meant just the positions available and people going into the graduate school. Before, like five years ago, it wasn't a problem. There wasn't a flood of now unemployable--

HANNUN: Five years ago, there was no acute problem, but I bet you if someone had sat down and run through the calculations, they should have predicted a problem, because at that time that's when a lot of hiring was going on, new faculty, and new funds. The system was set up for plenty, when there was a lot of demand created by the research dollars poured in by the government and very little supply. Government was supplying construction, fully funding research, and that was the mode. So departments started being created, and new faculty were being hired. That's still going on now, even at Duke.

As you look outside my window now, there's a new building coming up. What does that mean? New recruits creating more supply? And more graduate students? Because with every new recruit you need to expand your graduate training program, because, again, like the RO1 is the backbone of biomedical research, graduate students are the backbone of individual labs. So this is more and more expansion. That was good in the sixties and seventies. It's not good now, I think. So the system is starting to crack real fast.

Other errors in projections-- I think the NSF [National Science Foundation] made serious errors in projections that there's going to be a shortage of faculty by the year 2000. They retracted that miserably last year. Those were very primitive, erroneous calculations. So a number of reasons, I think, have worked almost in concert at the same time to really put major force on the RO1 system. And again, study sections which appropriate or approve grants and rank them were designed where peers can go in, review grants, and decide, "This one-third is great, this one-third is lousy, and the middle third, well, we can fund some now, give the remaining a chance. They'll come back. If they're on the right track, they'll prove themselves." So ultimately they were funding a big percentage of [proposals].

HATHAWAY: Wasn't it even like 50 percent at some point?

HANNUN: I think 50 percent from first round and maybe up to 70, 80 percent being funded. You know, if you consider--

HATHAWAY: Of the approved.

HANNUN: Of the approved, and going back, you know, second cycle or something. So the system was very generous, and the results were phenomenal. I mean, the expansion in basic research has just been phenomenal. I should actually distribute the blame where the blame should be distributed. The scientific community-- I mean, I've blamed now the university administration for not realizing the new times and what the new forces are and Congress for micromanaging and missing the point. But also the scientific community for playing the game and not making sure that even early on when things were plenty that they make the case for what their case should be.

Let me explain that. If I was a researcher in the seventies-- I could be a biochemist studying E. co/i. would send a grant to NIH and preface it by saying, "If we understand how E. coli do function x, we'll help understand cancer," and they would get funded through the National Cancer Institute. They knew they had no interest in cancer. Their work was not going to lead in sort of any legitimate connection to cancer, so that any independent outsider, if you really look at it, could say, "That's not going to tell me anything about cancer." So they played the game. They played it as people who did the research and applied for the grants and as people sitting on study sections funding those grants. They ignored that. They were instructed not to look at the relationship of research to really the health issues directly but just evaluate the merit, which is fine. But by playing that game, I think they forfeited--

HATHAWAY: We out there whose supposed tax money, to put it in the kind of context you're doing, think that "Yeah, those guys who say they're going to help cure cancer are going to do that."

HANNUN: And where are the results? That's the question now raised by congressmen and people. Where are the results from that E. coli work? That's where the scientific community, us, the scientific community, have forfeited a lot of our input into the system.

HATHAWAY: Why do you think that--? Why is there just "Okay, the NCI [National Cancer Institute] has got the big pot of cash now, so you make this up." Instead of going down the straight and narrow path and saying, "Look, we want you to set up the National Science Foundation's subdivision of basic pure research and fund that. This is why. We'll show you why."

HANNUN: Exactly. I mean, everybody was playing the game--the congressmen, NIH, the scientists, the universities. I mean, still up to this day my operation costs Duke probably nothing. My salary, the salary of everyone in my lab, all our research supplies, expenses are paid by my grant.

HATHAWAY: As a matter of fact, you probably bring in money.

HANNUN: Oh, I bring in indirect cost rate that goes into administration and overhead.

HATHAWAY: Which are actually pretty low here, or they were in ‘89.

HANNUN: They’re like 50 percent. That’s not trivial.

HATHAWAY: It’s 78 percent some places.

HANNUN: Everybody was playing the game. And instead of the scientists saying, “Hey, science, by providing the infrastructure, cancer researchers will benefit a lot, the economy will benefit a lot. We will be the leaders in biomedical research, and the economy is going to get a boost. The nation is going to get a boost because we’re going to train the best minds in this country.” That should have been the argument.

HATHAWAY: And it occurs-- Something like the National Endowment for the Humanities. I mean, people are editing Latin texts written in the fourteenth century, and they’re justifying-- I mean, somehow they are.

HANNUN: Oh, people would have justified that. I think they should have said exactly like you said. That would have been a very viable model, to say, “Well, let’s restructure part of NIH like NSF and fund basic research, knowing that if we understand how DNA gets clipped in E. coli we’ll have restriction enzymes.” You can’t foresee what’s going to happen, but you could make the general case. And then you prove it by example, in retrospect, saying, “By understanding restriction enzymes, we have the molecular biology revolution. Cancer research will definitely benefit and has benefited from that.” But, you see, scientists didn’t make that argument.

HATHAWAY: They just were too busy with other things.

HANNUN: They played the game.

HATHAWAY: I mean but why? Here’s somebody-- I think of you and actually everybody I’ve

interviewed. They'll always say, "Well, I don't want to make that generalization because I can't back it or I don't like to go--" You know, they're very, very careful people about making statements of fact and moving from point to point. That's the currency in which you trade. Why would they just give it up and--? And I've seen-- I mean, it's not in the seventies. I've seen grants where I know it's phony. I know it's this thing--

HANNUN: Yeah. And if you know-- You're the taxpayer. If you're a representative of the taxpayer, I think that's where the trust has broken down. Why did they do it? I think that was the game in town. It was sanctioned by everybody. NCI was happy to have the best minds in biomedical research being funded by NCI, so they didn't mind that. The system, as I told you, was not set up to say, "Hey, this is not NCI material. This is pure science. Let's create a pot for basic research." Those were the available funds. I think researchers went after the dollars.

Now, in the big picture, you can say by pouring in the money into NCI you did recruit the greatest minds into cancer. You know, basic research made them survive, provided the infrastructure. So to me it's justified. The thing is that not making the case has discredited us. I don't think playing the game is really the evil. In fact, those people that you mentioned, where it looks like it's really phony, those people probably don't play the game well. [laughter] No. I'm serious. Because the game-- To explain the situation, I think the game does not ask you to make a phony statement that "Hey, my work is related to cancer research through this and this and this way." Because who are the reviewers? The reviewers are scientists who actually, if they smell any phony part, they're going to discredit you a little bit.

HATHAWAY: I also on tape have situations or discussions about the fact-- Well, "I write my NIH grant. And really my NIH grant has three parts. There's one part, the first third, which is 'I've already done this. See what I've done? This is really good.' The second part is 'This is what I'm doing. See, it's going to pan out. It's starting to pan out.' And then there's this other little part, the third part, that's kind of really totally buried: 'Here's the stuff that I don't really know about. I'm really not even going to talk about it. But, indeed, I'm really going to use part of my funding on that.'" But I'm talking about, you know--

HANNUN: For cancer research? To relate to cancer research? Is that what you're saying? Or to relate to arthritis?

HATHAWAY: And then they'll say, "When I sit in on a study section, I read that grant, and it's written the same way. I know exactly what's going on, and I fund it."

HANNUN: But, see, those people are really not playing the game well, because, you know, I sit on study sections, too, and if anything, when you start pulling in those weak aims of your research, it starts sinking your proposal. The other parts must be really good to maintain it at the

funding level. But if you didn't put that in--

HATHAWAY: I think the work is brilliant work, but what I'm saying is that they think they're playing a game about, for instance, not taking risks and making it look like its going to save someone's life.

HANNUN: There are two components here in what you're saying: One is about not taking risks. That's unfortunately a reality now. If you get a reviewer--and there's a lot of mediocrity now among reviewers--they cannot take risks because they can't even imagine what's going on. We are facing mediocrity in science. I want to come back to that. But the other component of your statement is to say, "I'm going to save human lives with that study." I sit on American Heart [Association study sections]. American Heart tells people, "You can discuss the relationship of your proposal to heart disease in a paragraph outside the proposal." But you see some people coming in with a specific aim, saying, "Well, I'm going to do these things in cardiac cells and heart cells and whatnot." It's such a phony and weak part that it only sinks down the grant. So you don't have to. What I'm saying is NIH does not ask you to make that phony claim for an R01. The reviewers are asked not to look for a connection. You will still be funded by NCI for whatever you present to NCI without making the phony claim. So scientists shouldn't have been in part of the deception game. That's not a question of deception. The people who were incorporating some of that, let's call it deception, in their grants didn't have to. It was a misunderstanding on their part of how the process works, I think. But the problem comes--

HATHAWAY: Yeah. I guess I don't want to imply on tape that I think that there's really kind of like out-and-out deception going on and now it's coming home to roost--the payoff. I was agreeing, however, with your getting into this situation where once things get really tight it's like people have just kind of waited and now the thing has fallen.

HANNUN: Maybe it's fallen, but I think where scientists failed is to make their case directly to the people, in Congress, and in funding agencies that "Protect the investment in basic research because it's for the benefit of the health and the economy of the nation." That is an undisputed argument, and it should have been made that way. I think universities should have said-- It's still not too late, because I think the scientific community has to go back and make those arguments. Because I read in Science someone claiming that no one died of general medical sciences, so we shouldn't fund the Institute of General Medical Sciences! To have a bureaucrat at NIH utter that sentence even half jokingly is kind of very descriptive of the problem, very symptomatic of the problem. I think the scientific community should come back and make the case for really describing the significance of what they do, that what they do is going to maintain a class, an echelon, of brilliant young scientists. That is helpful for the economy, helpful for future health discoveries, and for health-related research.

HATHAWAY: And of course these issues go beyond just biomedical-- I mean, look at the issues surrounding like the funding of the space station and the [super conduction] super collider and just the almost kind of-- It's become violent, almost, and everybody's involved, and the American public is engaged in it.

HANNUN: The problem is you get something like with the [William J.] Clinton administration, which says we want to invest in the future of the country in the areas of the strength of the country. That administration sees clearly microchips as an area where we are ahead, and we are ahead, and we should invest in that and keep training people who are brilliant in that area. But that administration doesn't see as clearly that biomedical research is equally important, probably more important as an economic investment. If you look at the pharmaceutical industry in this country, the biotechnology industry, the university industry, I mean, we are clearly in an undisputed leadership position. I mean, with microchips, we're in a race with Japan. In biomedical research, were in a race with no one. We're clear leaders. We export to the rest of the world our abilities and accomplishments. I think the university should readjust and say-- The universities that want to make a commitment to biomedical research should invest now in that and say, "Okay, we want to keep active biomedical research programs. We're going to invest in building buildings"--if that's what they need to do--"and supporting programs," instead of saying-

HATHAWAY: Instead of just expecting it to be a cash cow.

HANNUN: Yeah, exactly. And the government has to, I think, dissociate the funding of health-related issues, where you as a taxpayer can read the proposal and say—

HATHAWAY: This is an epidemiological study about preventing--

HANNUN: Yeah. This is health. Or this person is looking at how molecules interact with the HIV [human immunodeficiency virus] so that they get imported or I can see the relationship. But then you say, "Oh, this is a pure science project. That's beyond my expertise in terms of knowing whether it's of merit or not. I'm going to let the experts decide on that. I don't need to decide on that. I don't need to give my stamp of approval for this particular proposal, but I understand that we should preserve and maintain this kind of science." Also programs should come in-- I think that's the last item of the equation. Programs in universities should come in and say, "Hey, a useful steady state for us, considering the budget limitations, is to have x number of young faculty coming into the system a year. That steady state. And really try to control entry into the system so that they maintain that supply of young investigators.

That's where, again, excellence becomes the issue here. This is where we'll regain

excellence, because if things keep on deteriorating we're going to lose the best young minds, because they're going to say, "Hey, there's a very great uncertainty in this career. I'm going to go into law school." The only way to overcome that is to say, "If you're excellent and you give it your all"--you know, all that you've got--"and work in that area, we're going to take care of you. You're going to be funded to do the best thing you can do, and you're going to have a decent life-style." Which, again-- I mean, scientists could be physicians. The best scientists could be. They don't go ahead--

HATHAWAY: They're not in it for the money.

HANNUN: Yeah. Although, again, the social climate has tempted many to switch to more financial--

HATHAWAY: I think we're entering an era also, clearly, where the lines that seem to have been drawn, let's say, between academia and industry and an investigator's self-interest in a project--his or her reputation, the reputation of postdocs and grad students in the lab, the peer review acceptance of the work, and now the starting of a biotech firm--have become fuzzier.

HANNUN: They're fuzzier, and there are a lot of contradictory directives and forces there, like government wanting to foster NIH relationships with industry. And yet NIH researchers, if they go to a company, they can't even get a bagel offered to them. You know, they can't accept a bagel. It's kind of--

HATHAWAY: Schizophrenic right now.

HANNUN: It is right now.

HATHAWAY: That's more, I think, a symptom of change, not so much a symptom of some disease that needs to be routed out.

HANNUN: No. That's a symptom of change. The same with funding. It is very symptomatic of change now However, those symptoms are sort of malignant symptoms.

HATHAWAY: But then you look at what-- And whether it can be correlated-- As I said to you off tape, the Pew program itself, in and of itself, and the people behind it and the board and Tom [Thomas W.] Langfitt and Rebecca [W.] Rimel are perhaps--and, actually, they've done oral

history--are, from my point of view, equally or potentially interesting people to talk to about this. Because all of a sudden in 1985 the kind of funding that you've just said on tape and I think almost everybody has, without exception-- You know, it is something sort of new and different. It's aimed at people at this one--I mean, it's very narrowly focused. It hits every big institution. I mean, somebody planned this, and it would be interesting to know exactly why. The way the selections are made is very different than most selections. It's fluid and flexible, I think.

And then the HHMI [Howard Hughes Medical Institute], which seems to be switching from "Okay, we're going to go to this place, build this building, fund these fifty guys and gals, and put them all together," and now they seem to be going around and just picking out individuals. mean, how HHMI perceives its role. And it's also just spending more money. I mean, it's in Russia now. So there may be responses to the malignancies or something like that.

HANNUN: These are very important, but they're only going to make a dent. They're maybe more like the equivalent of pain relievers in treating a cancer patient. You need more of those. It's very good that these are a couple of things that recognize and reward excellence, but you need it at other levels too. I mean, you may need it for more senior people, to tell senior scientists-- There isn't anything in the system at this point to reward a senior scientist at any level that makes a dent in the system. You reward them with a Nobel Prize or a couple of other major awards, but that doesn't make a dent in the system because all these awards go to the top .05 percent. That really doesn't make a dent in the system. But you almost need to award excellence at an advanced level, where you can say, "Hey, you've trained a wonderful cadre of young investigators. We're going to reward you." To the point where you know that if you do that, you're going to be rewarded. You know, with a Nobel Prize, now it's like touch and go. You could be the most wonderful, fascinating scientist, and you'll never make it, just because of the volume. So the. Nobel Prize I don't think should be a goal because, again, it's--

HATHAWAY: Yeah. I don't know that it-- Well, I guess I get the sense that like any kind of daydreaming goal, it's a goal--

HANNUN: But therefore it loses its effectiveness in rewarding excellence. So you need other rewards that can touch more people and reward them for different aspects. You can award the megalabs for their productivity, but you need to reward maybe the smaller labs. Phillip Majerus has trained maybe half of the academic hematologists in this country.

HATHAWAY: Who? I didn't hear the name.

HANNUN: Phillip Majerus.

HATHAWAY: Thank you. Now I recognize the name.

HANNUN: He's either trained directly or indirectly, you know. People who he trained went on to train others. Reward someone like that. Maybe his body of work has been excellent but never super-outstanding, but his pedigree, his contribution in terms of future scientists, I think is unmatched. Reward that, and reward the top 10, 20 percent who do that. Reward the top 10, 20 percent who contribute new creative thoughts to science. Those are still very much needed at entry level, like the Pew does. Maybe at intermediate levels, at later levels, but I still think we need to tackle things at the root. I think obviously now the country as a nation is not ready to keep expanding the biomedical research base the same way it's been expanded in the last twenty years.

HATHAWAY: It obviously isn't. I mean, perhaps that's kind of all of a sudden why there's some--

HANNUN: But rather than have sort of a scientific massacre five years from now, try to anticipate—

HATHAWAY: And have these new buildings be empty or something.

HANNUN: It's funny. Like my chairman already mentions the fact that the Department of Medicine, which is going to get a lot of space in this huge building right outside this window here-- He doesn't plan major recruiting into it because he realizes now that he's not going to have the dollars for startups for new investigators and at the same time give funding for scientists who miss one round of funding or were going to miss more than one round of funding. So I think reality is going to sink in. That's why I think building is kind of stupid now.

HATHAWAY: Yeah. But this was probably planned, what, seven years ago?

HANNUN: No. It was planned three years ago, two, three, no, two years ago. It was thought of maybe three, four years ago, but really planned two years ago. So I think the reality is going to catch up with us. But what I'm afraid of is, in the process, we're going to sacrifice the excellence in science. That's my concern. I'm pretty sure ten years from now, if things continue the same way that they are--let's say maintaining the same kind of funding--things are going to come back to a different steady state. We're going to see many schools bail out of the research game. They're just not going to get funded, and they're not going to have the ability to support research.

HATHAWAY: And maybe they got into it for the wrong reasons--they were getting money for it.

HANNUN: Yeah. From indirect cost and the prestige and whatnot. We're going to see bigger schools scale back on what they have. But what I'm afraid is in the meantime we're going to sacrifice excellence. We're already doing that. The message we're sending to our high school students, I've seen it. Mike [J. Michael] Bishop, the Nobel laureate, who came here a couple of weeks ago, spent quite a bit of his lecture to describe that.

HATHAWAY: I was going to bring up that lecture, because I heard it in Hawaii, I believe.

HANNUN: You did? Oh, okay.

HATHAWAY: Actually, I was disappointed in it in some aspects, but maybe we'll find that it is this-- We're getting toward the end [of the tape]. There was one question I wanted to follow up on and kind of ask you.

HANNUN: Do you want to stop now or continue with that--?

HATHAWAY: I think we can go two minutes. I mean, I'll just make sure I catch it [the tape].

HANNUN: In his discussions with high school students, the word has filtered down already that this is not the sort of career that people want if they want to be creative and productive. So we're sacrificing that at that level--entry into the system. We're sacrificing excellence at the level of people already in the system who are outstanding and excellent, in terms of really preventing them from being creative. I consider myself a successful scientist. The amount of time I spend in grant writing, in management, in doing things I don't care about, is overwhelming. What is the time that's given to allow for that? It's the creative time. It's the time when I can sit and read something really different from what I'm doing and get new ideas or times when I can go down the hallway and talk to someone, spend an hour. I don't have that time anymore, not because of—

HATHAWAY: And you think that's increased? In other words, that maybe like the generation before you was doing less paperwork and more--?

HANNUN: Oh, much less paperwork. And they would send one grant in, be funded four, five years, minor modifications, be funded for five years. I mean, now I probably have to write one grant, make sure I write a couple of others to send to other places, just to make sure I get the funding. So it's cutting back on the creative time. It's cutting back on what I propose in my grants in terms of creativity, which is a point you brought up. The peer review system is really suffering from mediocrity at this point in time. That's scary.

HATHAWAY: That's what I'm going to come back to. You kind of suggested, in a way, that that's still the one thing you want to see kept in place. In other words, that there has to be a reworking of it to convince the public, the taxpayer, that "Yes, okay, that's an epidemiological study. It's clear-cut about its health benefits or payoff, but you've got to trust us on the--We'll come forward and admit there's no direct correlation." But still it's too-- You know, it's difficult for the nonprofessional or the untrained person to do that.

HANNUN: I would still admit that the untrained professional should not evaluate even the epidemiological grant, but I think the untrained professional will see the relevance of the epidemiological grant. What I'm saying is the nonprofessional should also accept the benefits, although they're going to be much more long-term towards the health of the nation and its economy, of the purely basic research proposal. In both cases, I think it should be peers who review the merits of the proposal.

HATHAWAY: I don't think that people who collect garbage should be reviewing R01 grants, and I don't know that people who get R01 grants should be telling people who collect garbage how to do that either.

[END OF TAPE 6, SIDE 2]

HATHAWAY: You had something you kind of wanted to maybe follow up that we'd been talking about. I guess you were talking about [J. Michael] Bishop's lecture.

HANNUN: The image or the conclusion there was how we're losing excellence in science. I enumerated a few things, like, in terms of what image science is getting now among high school students, how creativity at the level of us scientists is being jeopardized very seriously, how our creative time is being eroded, how our creative thoughts are not being accepted in the peer review system, how mediocrity has crept all over the review system because of a number of reasons. One is many of the senior scientists--where the Pew [Scholars Program in the Biomedical Sciences] committee would be quite a good representation--have bailed out of the NIH [National Institutes of Health] review system. I think as a product of the eighties a lot of them have gone into spending their time forging ties with biotechnology and industry, and

they've really bailed out of the NIH review system. They are the ones who could look at a proposal that I submit and evaluate it the way the Pew does in terms of "What is it this person does? Is he trained adequately? What is he proposing? Can he do it? And is it exciting, is it unique, is it something that's going to help science?"

HATHAWAY: With this NIH grant, though, I mean, that's clearly something they've given-- You just don't think the people who sat on the committee are qualified. I mean, they do talk about how you're new and whether you look like you're capable.

HANNUN: You're bringing up my particular grant proposal to NIH and that particular study section. This is physical chemistry or physiological chemistry. This is one of the most rigorous study sections. I think if you read the critique you would have found that it is a very rigorous critique.

HATHAWAY: Compared to some of the other ones I've seen, I actually can follow it from sentence to sentence.

HANNUN: It's a very rigorous critique. I have no problems at all with this kind of review. And if you look at the study section members, it was pretty much senior people in biochemistry.

HATHAWAY: Actually, somebody went through them at some point and actually marked a check--I don't think it's a rating thing--marked check marks and then "new." And so I guess it was just a question of knowing who was on it?

HANNUN: Yeah. Something like that. But I had another R01 sent to a hematology study section, which is much more representative of other NIH study sections. I didn't give you a copy of that. I got funded through that, but the quality of the review was mediocre. They still funded me because I think I had a very strong proposal and I had done a lot of the work. Sort of anticipating that, I had written it that way. But that's not a study section I want to entrust my future in science to.

HATHAWAY: This one started in '93, if we can just use your situation as a particular and then back out to some more general discussions, because I think there's more that we'd both like to cover, although I think I let off a lot of steam off tape--a good thing. This is your interview, not mine. It started in, I guess, June of right? No, no. They met-- Okay, so the funding didn't start until '91.

HANNUN: Yeah. I think either December ‘90 or January I forget the--

HATHAWAY: Okay, and then you submitted it in ‘89, I mean, a good year and a half before. And I guess it was reviewed, and you were asked to--

HANNUN: Yeah. It was reviewed, and it was right at the borderline. I think I got 16 or 17 percentile, and I had to move up to 15 to get funded.

HATHAWAY: Okay, and this is what this-- Yeah. It says 15.7, I guess.

HANNUN: Yeah, that’s the percentile ranking.

HATHAWAY: They’ve just divided by ten the score, right.

HANNUN: Oh, no. This is actual ranking. You know, per hundred grants, where does it rank in the hundred grants, all grants.

HATHAWAY: And this 157 or 15.7 was the one that-- That’s the original score it was given, or is this the result of the resubmission?

HANNUN: This is the result of this--

HATHAWAY: Again, not to bring up anything bad, but with the news about or the gossip about that this year or next year, the first fiscal year of the Clinton administration, there will be 10 percent funding-- This wouldn’t-- I mean, you’re not going to apply again until ‘95, I guess, right? But this would be-- There would be a chance-- I mean, I know some study sections get fewer applications and they can fund down to the hundred percentile.

HANNUN: It’s all going to be funded by percentile, so it doesn’t matter how many applications a study section gets. So that’s why they rank them.

HATHAWAY: So if there’s none in the physiological chemistry that got above it-- Yeah, okay, I see. Is that something you’re aware of or think about? Or do you think that your percentile ranking will be much better because you’ve established this grant and the Pew established your

work? And now some of the reservations they had on this one, that you're starting out and you seem to be doing too much or trying to--?

HANNUN: It is a major concern to me. It's a concern. don't know how major. I think with what we've accomplished on this, we've really accomplished a lot. In normal times, I think I would rank real high with that and be funded. However, again, these are not normal times, and the system, as I mentioned before, has not really been set up to discriminate the best 10 percent from all the others. It's been really set up primarily to discriminate what should not be funded. With 10 percentile you're talking about grants in the outstanding category not being funded.

HATHAWAY: Oh, yeah. I guess people feel that in even 20 percent that they are--

HANNUN: Remember, there's a category of excellent, and then there's a category of outstanding. So excellent are definitely not getting funded, and even many outstanding are not getting funded. My concern, again, with the mediocrity of study sections, is the attitude has shifted in funding. The way they would look at it is not whether this is fundable or not or how exciting or not, but the attitude is "What can we nail this grant on?" In a way, it's trying not to fund anyone if you possibly could.

And to be able to do that you need any justification. So if you can find something to shoot down the whole grant with, that's what they're doing. They're shooting down whole grants based on anything they can.

HATHAWAY: Have you done any ad hoc reviewing, any study section for the NIH, for physiological--?

HANNUN: No. I haven't done--

HATHAWAY: Not for NIH.

HANNUN: No. Not for NIH. I've done program projects for NIH, but I haven't done--

HATHAWAY: These are like site visits or--

HANNUN: These are like site visits and reverse site visits, both ways.

HATHAWAY: I'm sure you'll get asked soon.

HANNUN: Well, I'm trying to avoid that.

HATHAWAY: Now, but you just also pointed out-

HANNUN: Well, I'm not senior. Maybe in a few years.

HATHAWAY: I'm sure you'd take the responsibility seriously.

HANNUN: When I say "senior" people, people who have been through it for some time, so they have the perspective and they can know that someone like me coming through the system-- They have some, I would say, gut feeling from experience. "Is this someone who is going to make it? Is this someone who is going to contribute original research? Or is that someone who is going to be stuck with different obstacles and really not be a productive member of the scientific community?" The problem with this kind of discrimination is you need to have the flexibility to fund 40 percent of grants or 50 percent.

HATHAWAY: And expect that you're going to fund the person who's going to have the obstacles and it's going to turn out to be kind of a dud, at least that one time.

One thing I just wanted to kind of follow through--I actually brought this up off tape, but I'll bring it up again. We don't need to spend a lot of time on it. You were talking about kind of your ideas about the reform of the system and the need of the scientific community to kind of push and be a part of this kind of reform. So that the public's perception, perhaps, and the way that they get funded actually reflects the reality of the work they're doing in its relationship to society. And that they had kind of gone along and played the game. Not that they were guilty of deception, but they played this game just for whatever [reason]. It seemed to be easier. Who knows? Everybody else was playing it. And I think you were emphasizing it as specifically for the more esoteric areas of basic and pure research, let's say, like theoretical particle physics, as well as biology, or lots of different areas within biology. And that really there is a gap between-- I mean, there really shouldn't be this kind of, let's say, lobby-- I don't really want to call them a lobby, but this breast cancer group.

Where really through political pressure and really direct action--civil disobedience, coming up with their own budget, writing their own proposals, and really taking over the agenda--they were able to get this huge, I mean, hundreds of millions of dollars set aside for specific kinds of funding.

I guess I wanted to ask you about that. You seem to find that that's not a good-- You know, again, not that breast cancer research doesn't need to be funded to the tune that they say, but just that that kind of situation is how it's coming about and that it's now because basic research is seen as being a part of this, right. People write grants and say, "We're going to help find a cure for breast cancer" or a way to detect it even or something like that. That these people who are not biologists shouldn't be in on it at that level. Of course, we're all in on it in some way. We pay taxes; we elect representatives.

I also asked off tape if you were familiar with Representative George Brown's recent piece on "the myth." I actually think maybe it was to get scientists all upset and to start thinking about it, as opposed to being real, given his past record. But he just comes right out and says, "This is all baloney. Basic research doesn't have any direct benefits for society. We need to start thinking about funding applied research." He even says, you know, "And in the social sciences we need to start, instead of this little NEH [National Endowment for the Humanities] thing that we give just a trickle of money to and this big NIH thing and this lots of money we give to--" He's talking about restructuring it so that economics is going to become the money-maker for universities or something like that. I'm wondering how you feel or what you-- George Brown is really taking kind of a radical position and coming right out and saying, "Not only should that stuff be allowed to happen, but I'm in a position to institutionalize it and to make it like the law of the land." How would you combat that or respond to--? I know that's a whole bunch of questions.

HANNUN: I haven't read the article, but I know sort of the gist of it. So I know what you're talking about. I think that's, again, part of the scientific community and university's not articulating their goals and the strategic goals of what they're doing and why they're doing it beyond the phase of scientific discovery. Because as I mentioned-- Or as a consequence of not articulating-- The dynamics is sort of more complex than that, but the infrastructure of basic research is really based on thin ice. On one side, you have the whole biomedical establishment-- universities and labs and research and investigators. And on the other side, you have Congress and the public. And the support-- The thin ice has really been built primarily by V. Bush, who was the adviser to [Harry S] Truman or-- Vannevar Bush—

HATHAWAY: Who is of course everybody's hero.

HANNUN: Truman and [Franklin D.] Roosevelt.

HATHAWAY: Yeah. Well, he, I think, had an important position by the end--

HANNUN: End of World War II.

HATHAWAY: Certainly by the end. So [adviser to] Roosevelt, perhaps.

HANNUN: Roosevelt and Truman. Then a few more enlightened members of Congress. That's not thick, deep support. It's been great that they had the power and influence to set up this gigantic biomedical research infrastructure. But everybody followed the line without articulating the long-term strategies. Universities went for it because it was a good source of dollars and prestige. They rank medical schools now by how much NIH dollars they bring in. So they're playing that game. Scientists play the game. And remember, these things dictate the shape of science, maybe not directly, but obviously indirectly they dictate the shape of science. If you're a cell biologist and you come to a point where you have an option of working with hormone x or y or cell type a or b, if you know that there's going to be more money in breast cancer research and one of your cell lines is a breast cancer cell line, you go for that cell line. So you're going to become a breast cancer researcher, even tangentially. But with time you will be part of creating the infrastructure for basic research in breast cancer.

So society does indirectly dictate the shape and outcome of science. However, by not stepping back and having universities articulate-- "Do we want to be a formidable center for biomedical research?" And if the answer is yes, "Well, what are we going to put into it?" Not just "What are we going to get out of the government for it?" "What are we going to put into it? What are our goals going to be? How do we modify those goals? And how do we modify our tactics if our strategy changes?" Well, they haven't done anything of that.

They just know that it's good to be prestigious, and it's prestigious if you have NIH dollars. "Let's get as many as we can. Let's get as many researchers so that they can get as many dollars as they can."

HATHAWAY: And you see that just across the board. There's not a medical school or a medical center like Duke [University Medical Center] or Harvard [University] or whatever that's done this for any other reason?

HANNUN: No. Then the same with the research community at the level of senior scientists and department heads and what have you who come and say, "Well, how much research--? Let's figure out, let's think through, how much research does our nation want to support for basic research?"

HATHAWAY: And have a say---

HANNUN: Yeah, and articulate that. They should have been articulating that for twenty years so

that everybody is in sync on that. So that exactly what Representative Brown is saying wouldn't come up because-- Actually, it's funny, because even two years ago I was trying to discuss these issues with someone. Everyone thinks I'm a pessimist, but I try to tell them-- You know, when I was telling my fellow Lebanese that their country was going to fall apart, they thought I was a pessimist. And when I say, "Well, let's be careful here. Maybe the whole biomedical research community is going to fall apart. Our support is thin--"

HATHAWAY: If George Brown's piece was more than just "Hey, wake up scientists," then maybe it's really thin, because he's--

HANNUN: Yeah. I hope it's just a wake-up sign, but—

HATHAWAY: I'll send you a copy.

HANNUN: Yeah. Please do. But I mean, I'm still worried about that, about a time when the breast cancer lobby starts clashing with the prostrate cancer, with the AIDS and whatnot, and when they finally say, "Hey, let's ax out all the Drosophila studies," you know, or all the E. coli or all the yeast genetics. "Let's pour all that money into--"

HATHAWAY: Applied research.

HANNUN: Applied research. We have to create deep support for what we do, but also beyond that deep support we have to define the volume of science we're going to support. We are at a steady state, I would think, in terms of the physical sciences--chemistry, physics, even biology. Universities have adjusted to that. They get some research from NSF [National Science Foundation], some from in house. They pay salaries. You know, they pay nine-month salaries for faculty. It's at a small scale mostly, except for very particular labs. It's at a small scale, but they're steady state. No one's going to dispute the department of biology in terms of, well, "We need the department of biology. We need research in biology." That volume the nation is happy with. But then we have biomedical research. No one has articulated how much we need of that.

You know, you look at Duke. I look at Duke and I think, "You know, the sky is the limit in terms of how much biomedical research they're going to go for." If there was no crunch in funding, I really would not see them even thinking twice about how much they want to grow. The more the better: the more the scientists, the more the money, the higher the ranking of Duke. We don't have a problem with land here. We don't have a problem with construction. So there was no problem in the social aspect and the civic aspect of "How much do we need to be part of biomedical research?" We haven't articulated that. That's why it's coming back to haunt us now.

HATHAWAY: It's kind of occurred to me, at least a couple of times, that also-- I even wonder about-- It's certainly been institutionalized, but why, for instance, so much of the molecular biology, molecular genetics, even cell biology that's being done is being done in medical schools and not in traditional [university departments]. I mean, of the really great places and really top-notch--

HANNUN: I think the bottom-line answer is money was available from NIH. That has to go primarily to medical schools. Medical schools knew they could access that money. They put up the buildings and brought in the researchers.

HATHAWAY: You can trace some of the-- I actually believe that I have no [knowledge] beyond anecdotal-type things, for instance, that this thing that is DUMC [Duke University Medical Center] and its semiautonomy from the rest of the campus and the university is due to its incredible-- It throws its weight around here. I know the case, for instance, of UCLA, that development of a medical school right at 1948, '49, '50. It's always been an issue of "Is the medical school going to take over the administration of the entire campus because of its clout?"

HANNUN: Yeah. I mean, I think it's obviously—

HATHAWAY: It's institutionalized by now.

HANNUN: And since now the winds are blowing in the reverse direction, or in another direction, I think rather than to allow this hurricane to realign things at a very great cost--I really believe it's going to be at very great cost--let's be more intelligent and everybody who is involved in it help redefine it. We should bring in the pharmaceutical industry, the biotechnology industry, because it's the same infrastructure for all of them. We have to be careful about that. One thing I'm disappointed with really is the ability of scientists to come together and discuss these things and articulate them.

HATHAWAY: They're so busy.

HANNUN: Well, I don't think it's that.

HATHAWAY: You think it's something more about being a-- I mean, I'll just ask, I guess, instead of trying to put words in your mouth.

HANNUN: As we talked off tape, in last year's Pew meeting I was almost horrified to see how scientists reacted to a Ph.D. [S. Wesley Jackson] from the Land Institute.

HATHAWAY: And this is an environmentalist-type—

HANNUN: Yeah. Environmentalist. He's a land researcher. That's what he calls himself. Many scientists were outright antagonistic to this guy. I thought it was a combination of arrogance, ignorance, and not feeling comfortable in dealing with these issues. Because I had very good discussions with this person, and I think we came to a common ground. And believe me, once you hit a common ground with the public, it's a point to take off. But scientists, for some reason-- I think you mentioned maybe they're all wrapped up in a cocoon now, and they've been protected, overpampered. They don't want--

HATHAWAY: I don't know if so much pampered but just this idea that "You're right, you needed eighty hours a week," and you've got to admit-- You know what I mean? By "coddled," I don't mean pampered but allowed to do it the way that--

HANNUN: To do it right in the current environment may take eighty hours, but I question the validity of that. I question whether this is the appropriate model too. mean, the British do it with probably thirty hours a week.

HATHAWAY: You would be an exception. Most people bring up the British scientist as an example of the blithering kind of thinking person who doesn't do any work. But I think it's an American-British kind of--

HANNUN: I don't agree with that assessment. There are formidable British scientists. Their support is dwindling; that's a different story. That doesn't say they're any lesser scientists. But I think they're actually forced to think more carefully about what they do because of the constraints on doing research.

HATHAWAY: I've talked to somebody who said the exact opposite, that there it's a situation where they don't ever want to be seen as kind of like being wrong, so they overdesign everything instead of just going out and doing it and maybe finding out the accidental discovery that would come from just doing a million--

HANNUN: That's clearly the American way of doing it, the Clint Eastwood way of doing it.

HATHAWAY: [laughter] Which has its other downside.

HANNUN: it has its merits; it has its downside. That's fine. But it definitely tells you that it doesn't have to be totally that way. My philosophical interpretation is that scientists have poor social skills. It's something I consider at the personal, family level, because I grew up in the Middle East and my children are growing up in the States, and there's a black-and-white difference in social skills and interactions that occur, I would say, not only in the Middle East but almost the rest of the world versus the U.S.

HATHAWAY: And the U.S. is--?

HANNUN: The U.S. is very nuclear-family-type, not much in terms of social fabric beyond that.

HATHAWAY: I'd except Germany but-- I'm just being mean.

HANNUN: There isn't much beyond that. Definitely the extended family has all but disappeared pretty much. Beyond that, the structure-- I mean, I think the mobility question-- With mobility, that means uprooting. That's equivalent, synonymous. You can't have one without the other. So while mobility is essential for economic success and individual success, it has uprooted the social structure, uprooted families and therefore the social structure. Now, the downside to that-- I don't think that per se is a downside. You know, I definitely want the mobility aspect because I favor excellence and having people matched with the best they can do.

HATHAWAY: Something I think is the theme throughout the interview.

HANNUN: But the downside, the obvious downside, is by having the nuclear family, things have turned around. So that with my children growing up, everything revolves around them. When I was growing up, I was almost on the periphery, and we had to find our way into--

HATHAWAY: It's not a children's culture.

HANNUN: It's not a children's-- We had to find our way into the social structure. I think that polishes social skills a lot in terms of being able to develop solid, long-lasting friendships, understanding of how society works. It seems to me that the superspecialization-- Well, first, the

upbringing does not necessitate, doesn't even require, the development of social skills. Most smart people will do fine because they're smart and they can learn real quick; many other people, though, don't. When it comes to scientists, I think they learn how to deal with their environment real well. But I guess because of two pressures, not just the pressure of needing to work very hard but also the pressure of not having-- You know, if you have to learn social skills beyond that, that's a whole new set of pressures and limitations to your ability to go and sit with other scientists and discuss the policy of science and the civics of science and how to organize scientists productively into going beyond their prescribed roles, going beyond what's dictated by Congress and universities and department heads in terms of "Well, this is the space you're going to work in. These are the funds you can apply to. This is what you can do." And I think a lot of it is, one, we don't have the time, but, two, we don't have the necessary social skills to look at it from a social perspective and say, "Well, this is a question of national importance."

That's my other hat, the clinical hat, and we're now facing an even worse situation on the clinical side. We're going to redefine how 10 percent of the GDP [gross domestic product] is going to be allocated, with clinicians and physicians playing a very marginal role in that, actually physicians and patients playing a very minor role in that.

HATHAWAY: And who's playing-- Insurance companies and pharmaceutical companies?

HANNUN: Well, who knows who Hillary [Rodham] Clinton—

HATHAWAY: Right. It's a big secret.

HANNUN: Yeah. Who's providing information, analysis, and whatnot. I don't know. But obviously the lobbyists are representing not the clinicians who are treating patients, as such, not that aspect of physicians. You have the AMA [American Medical Association], which is presenting the more sort of business-type physicians. You have the health insurance industry. You have the lawyers. You have the whatnot. And yet this is talking about 10 percent of the national economy.

HATHAWAY: You mean the total spent on health care.

HANNUN: Yes.

HATHAWAY: No. It's actually like 17 percent now.

HANNUN: It's 17 now. Geez. Last year it was like 10 or 11.

HATHAWAY: I think I just saw 17 percent in the paper on Sunday.

HANNUN: Maybe that's a projection or something.

HATHAWAY: Actually, maybe it is, but 14 percent for sure this year or last year.

HANNUN: That's amazing. But then this is dispensed at the level of the physician and patient, and they're almost out of the picture. And, again, it's poor social skills. The physicians haven't come-- You know, they're busy too, but it's also poor social skills. They haven't seen the social implications of what's going on and come and said, "If you want to maintain excellence in clinical care, this is our say in it."

HATHAWAY: It's funny. There's a report in the New York Times asking people what they thought doctors made and what they thought they should make. And they underestimated by half what they think doctors make, and then they say that they should be making about half what they underestimated they're making by half! It's almost automatic, if you mention the AMA, that anybody who has paid attention or has had an experience now where insurance is hard to get and they're not having regular medical care anymore--and that's a lot of people--the response is "AMA, they're evil." I mean, it's gotten to a point where what you're saying has clearly gotten to a level of--

HANNUN: Well, instead of the physicians who work with patients directly, which, you know, the bulk of-- You know, this is the primary hat of a physician. Instead of organizing around the patient-physician relationship and administration of health through that, the only organization is that created to protect the business hat of physicians. That's given us a very bad press.

HATHAWAY: Very bad.

HANNUN: Appropriately so. When the AMA starts supporting one congressman over the other and pouring in money as just any other lousy lobby--

HATHAWAY: It's a special interest group in the eyes of-

HANNUN: It's a special interest group. And what physicians should have done is say, "Yes, be a special interest, but in the interest of the patient-physician relationship." That's the interest that should have gone in. I think if society comes to grips with it, it will approve a decent--not just decent, a lucrative--salary for physicians. But you don't have to make most physicians into millionaires., Most students who come through that I work with, that's not their ambition. That's something that builds later in their careers because they see it as an opportunity.

HATHAWAY: To become a private corporation.

HANNUN: Yeah. So I think it has as much to do with being busy and superspecialized as with the lack of social skills.

HATHAWAY: It's interesting how although we were just a little bit before talking about the rather almost opportunistic attachment of basic biomedical research-- and we call it biomedical research, interestingly enough--to something like where the money was, I see the other effect as well, the superspecial-- I mean, in some ways it's not unnatural or strange, and it's not just a bunch of people with their financial hats on thinking.

HANNUN: This is how the free market works in this country. It's not totally free. Society dictates some priorities and pours in money there and then free market.

HATHAWAY: And as I think I said to you on tape very early on, or maybe off tape--maybe it was to Dennis [B.] Lubahn--I really think that we're kind of documenting a lot of this by the people who participate. There are a lot of M.D.'s, in your year especially, who are doing basic-- Really, talk about wearing hats. That's an image you've used, I mean, a phrase you've used, without my prompting, and actually every other M.D. I've interviewed so far. I'm sure it's something that I think you're all aware of. Who knows, maybe you talk about it with each other. I'm not saying you Pew scholars but M.D.'s. This is a vital concern to them because they're involved in it. But perhaps once they're involved in basic research, we see their medical hat off every once in a while and they have the other one on. Very interesting. I don't know. I mean, actually, I could go on for days.

HANNUN: I hope not.

HATHAWAY: No, no. And that's what I'm going to say. don't have anything absolutely vital [to ask] about funding your work anymore. I mean, I think we've come to the point where we need to-- Unless you feel you need to add a few more things.

HANNUN: On my work, we talked a lot about the sphingolipids and how I thought that fit the whole thing. I didn't talk about the protein kinase C work.

HATHAWAY: And I promised we'd get back to it, and, of course, I lied.

HANNUN: Well, I just need a minute to describe it, just to contrast it with the sphingolipid side because the sphingolipid side has been purely biology and discovery. The protein kinase C side has been what we talked about the other day in terms of taking things at the molecular level but still within the cell to look at function. I don't want to spend too much time on that, but we're starting with a much more advanced background, information, and database with protein kinase C. As you mentioned a little bit, there was so much going on with protein kinase C. Yet we think we've sort of attacked aspects that have been more or less not looked at with protein kinase C and not examined in terms of—

HATHAWAY: And that they're fundamental. That it's not just "Oh, protein kinase C is involved." I mean, it gets reacted--

HANNUN: Yes. Not this-and-that biology but more in terms of how the enzyme works in the cell. We have evidence now that it binds proteins, that it gets phosphorylated by other kinases. These are things that regulate individual isoenzymes of protein kinase C. Rather than look at the whole family as one entity involved in a biologic process, we're coming down now to the molecular interactions that define the function of each isoenzyme, because each one is an entity on its own. So that's where we're heading with that. I mentioned that because this aspect of the lab has provided very complementary conceptual and practical skills to the sphingolipid side of the lab. We have some very advanced methodologies and techniques in molecular biology, in protein biochemistry with protein kinase C. While with sphingolipids we've started with a very physiologic-biologic point, and the work on protein kinase C has helped us move with the sphingolipids very fast whenever we come to a molecular level. I think that's the extent of how I want to describe our research. I think I described how I work with my students, too, in terms of working--

HATHAWAY: Right. No, you did. I think it's been very thorough on the level of theoretical, philosophical, as well as the guts, you know, what happened. I think you have a leaning toward talking about it in more general terms, and I think that's actually the gems that I'm looking for. I don't want to ask you to go through this step by step. People can read the publications. That's what they're there for as well. I did have one quick question. Are you really the only bridge between the two--? I mean, are you the one who has all this perspective about how the two sides of the lab or the two labs work? Or have you got people who are--? I mean, are you inculcating this view and perspective into students?

HANNUN: Not much. The only person is my wife [Lina Obeid Hannun], who is my collaborator, who partly trained with me--

HATHAWAY: And that's where we're going to move next, to your family, so this is--

HANNUN: Yeah. My wife is my collaborator. She's now an assistant professor, and so she's in faculty. She has just set up her own independent research. We sort of still collaborate on a lot of things, but she has a few things on her own, I have a few things on my own. She's the other person who has now that additional perspective, but that's about it. I think it's too much to ask students at this point to have the perspective of—

HATHAWAY: But nobody's seen it. I mean, has anybody come up to you and said or you've gotten a letter from somebody saying, "Hey, you know, it's kind of interesting because--"?

HANNUN: No.

HATHAWAY: I mean, I noticed you've published-- Well, I think even in the same issue of like the JBC [Journal of Biological Chemistry]-- But, you know, kind of the two sides, two articles. I mean, not next to it, but anybody who is astute enough to figure this out might say, "Wait, there's these--" I certainly looked confused when I first started calling up your name on MEDLINE [medical database].

HANNUN: I haven't had that yet. I mean, I'm invited many times to talk about sphingolipids, a few times about protein kinase C, but it's either one or the other usually. It's either one or the other.

HATHAWAY: We were just talking about hyperspecialization or something like that. That may be, actually, it occurs to me, another reason for your not letting go, even if it's starting to be tense or too much work or you understand that you're hitting a limit of saturation, that to let go of that is to admit that you have to superspecialize. Keep up the fight, right?

HANNUN: The other thing is the biology. I think as we've pursued sphingolipids, the biology is just totally fascinating. As we have pursued protein kinase C, the biology is not less important. We use platelets as a model a lot, and the implications for atherosclerosis, for ischemia, for heart attacks, for strokes are just very important. That's another reason not to let go of that. In a way,

again, there's a bridge that's still missing that we would like to somehow get into in the future by, again, building those molecular blocks basically.

HATHAWAY: In a sense, we have a time limitation, but we can come back after your appointment, and we shouldn't hesitate to do that. One thing I know you wanted to talk about, and I would like to as well-- And we don't have to do it from the point of view "Oh, Dr. Obeid is your collaborator, so we have to talk about her." We can just talk about your family, and so we'll talk about her as your wife and your three children. I'm not going to come up with a question to ask you. It's something you said you definitely wanted to talk about.

HANNUN: Well, I want to talk about it because, again, as you mentioned, we talk about the background and then the science, but, again, to put it in perspective--

HATHAWAY: And then I lose sight of the other parts of your life.

HANNUN: I think my family is an important part of my life. I don't want to rank order them. As long as my kids [Awni, Marya, and Reem Hannun] are healthy, I want both. If my kids are not healthy, I'm ready to give up science without a blink. But my family is a very important part of my life, and I've structured a lot my activity to fulfill my family obligations.

HATHAWAY: We met on a Friday, and of course we didn't meet over the weekend. I mean, as an example of-- I'm not bringing that up to kind of-- Just to indicate it-

HANNUN: No, that's true.

HATHAWAY: I remember the first time I talked to you on the phone, you told me you "don't do weekends," not for this sort of thing.

HANNUN: Yeah, well, I don't do weekends for almost anything unless it's my month of rounding on the clinical service. I also go home early two days a week and take care of my children.

HATHAWAY: There's an explicit sort of agreement between you and your wife?

HANNUN: There is. It's something that we've worked out.

HATHAWAY: There are no rules written down.

HANNUN: There are no rules written down, but that's something-- I mean, I wanted to be involved, and she was getting too much pressure just handling the family all by herself and a clinical career and a research career.

HATHAWAY: And triplets. I know you already mentioned it, but we should emphasize that, I think.

HANNUN: A lot of my civic concerns, my concerns about excellence, the future, derive a lot from making sure that my children have even better chances and options than I had. I don't think I need to belabor on my family beyond that.

HATHAWAY: If you want to kind of just say, "That's it," I actually have a few questions more—

HANNUN: Yeah. Go ahead if you have specific questions, but I just wanted to put things in the right perspective. Well, the other perspective is that my wife and I collaborate. We haven't come up with any formal arrangement, but we can talk about work at home or we don't. I know some couples have an arrangement where they don't talk science at all at home or other arrangements. We're sort of feeling our way around that. At times it does tend to be exhausting, you know, when you're doing science around the clock.

HATHAWAY: It's a very common phenomenon, however, that scientists marry-- And I don't mean a physicist marries a geologist but--

HANNUN: Within a similar discipline.

HATHAWAY: Right. You meet them-- I mean, your life is--You didn't meet your wife-- You met her in high school. Well, maybe there wasn't a romantic attachment.

HANNUN: No. We just met in high school.

HATHAWAY: So it was med school where the romantic-- I don't want to get into the nitty-gritty of dating and hand-holding or anything like that, but I would be curious--if you do want to talk about it--to get some sense of both your consciousness about being in the same field-- Obviously, this was back in Beirut, so before definitely either of you had any idea of research and basic research as the path you were taking and whether this-- Not that there were struggles and working it out, but just how you-- Was it just something you decided you would not deal with that way and that kind of it advanced just as things came up?

HANNUN: I think we pretty much independently developed our careers, if that's your question. I'm very sure there are subtle influences and maybe very strong subtle influences from one of us on the other, but it was never sort of "Oh, I'm going to go into science. How about you also going into science?" Or "I'm going to stay in academics. How about you staying in academics?"

HATHAWAY: "I won't leave here for twenty years because you've got to stay here." I take it, when you came back to Duke, it did hinge upon whether your wife could do something here as well.

HANNUN: Yes. Absolutely. And we're playing it by ear now. If one of us finds a position, it would be contingent on the other finding something acceptable.

HATHAWAY: It's happened here, and that's not always easy to do.

HANNUN: Yeah. Exactly.

HATHAWAY: The other thing is I was curious--and this may reflect my own ignorance--but one of the concerns of what we're trying to collect here is just the changing face of science, and two areas, of course, are the continuing acceptance and the push for representation of what we'll call minorities and women. I think your lab is a good--I mean, if I look at the names, which is the only guess I'm making, I get the sense that this may be a conscious kind of thing for you as well.

[END OF TAPE 7, SIDE 1]

HATHAWAY: And so I'm curious. I wonder also about just the situation. That's normally kind of thought, "Oh, husband and wife, they collaborate." Well, the husband's at this [high] level, and the wife is a research assistant or a postdoc or that sort of thing. Whether you've dealt with these kind of issues on, again, a conscious level or it's really not been and it's just all turned out

this way.

HANNUN: The issues of women and minorities in science? I think that wasn't a conscious effort to do that. It's actually something that I'm amazed at. I definitely see heads of labs not comfortable taking women. I've never had that feeling, so I think it's almost like the reverse. Where women feel that they're going to be comfortable-- Probably there aren't many labs.

HATHAWAY: I was going to say, actually, perhaps even at some points you've had where, of course, more--

HANNUN: I've had in my lab more women than men, for example. I have minority people in my lab.

HATHAWAY: And again, you're not out looking for them. You find each other for other reasons.

HANNUN: The other thing is-- I mean, a reason that women can be discriminated against in science is many lab heads are very aggressive in that--

HATHAWAY: You mean in general and the way they are as men or--?

HANNUN: No. In the research activities. They look at women with some uncertainty in terms of "Well, can they be as aggressive as men in research, and are they as committed long-term?" You know, it becomes a self-fulfilling prophecy: "If women don't make it up in science, maybe they're not as aggressive, and if they're not as aggressive, I don't want to take them in my lab." Maybe they bail out when they get pregnant. Maybe they bail out when they get married and they move with their spouse. We always look at the woman as the one giving in in any family situation. I think until that changes it's going to be very difficult to change the perception of women as always the weaker link. I've heard it from other people, saying, "We don't take women for that reason."

HATHAWAY: So you've never had a woman six months pregnant come and say, "I want to be a postdoc," and you thought, "Oh, she's pregnant. She's married this guy. Her husband does this--" You just-- If she's talented—

HANNUN: Yeah. My philosophy is-- That's, I think, how I started my research lab, because I

didn't-- I mean, Bob [Robert M.] Bell is very respected in his field, but that's not a very glamorous lab. And my area of research obviously, at least for many years, was not glamorous. We had to build from scratch. My philosophy was to work with every person so that they can execute their potential, not my expectations, and work with them on that. I've worked with many people with different kinds of abilities. I'm happy with what they achieved. I don't think many of them were superstars, but all of them were committed. They wanted to be scientists, and I helped them achieve their potential. That's made my program successful with whatever I-- As long as people were sincere and honest and willing to learn and work.

HATHAWAY: I guess I'm coloring the conversation. guess I see that as not the common way that labs are built. Would you--? Or you just don't know enough other people's--?

HANNUN: I don't know enough about others. But I see many labs that wouldn't take women, for example, or many labs that would accept [only] the best student or no student or the best postdoc or no postdoc. There's obviously a lot of merit to that because you get the most productivity and the most exciting interaction but—

HATHAWAY: If you get the sexiest topic and if you can turn down thirty people, you've got that luxury. I suppose if you had a huge waiting list, you'd think about picking out the people who looked like--

HANNUN: Yeah. Let's be realistic. But there's always, I think, room to work with anyone who wants to spend their career in science.

HATHAWAY: And another thing--and this may be of no interest to you--as somebody who is-- I mean, I just don't know. Would you say that since your attitude towards women seems to be a lot different than I guess we're talking about American men or white men or whatever we'll call them-- I suppose that almost sounds terrible to call them that. Do you think it's cultural? I mean, your upbringing perhaps? The politics of maybe—

HANNUN: I grew up in a rather chauvinistic society but not totally. I was surprised, I still am surprised, that a lot of American men are chauvinistic, basically. It's surprising. Many men, even in leadership positions, are not comfortable working with women, either as their subordinates or their superiors. Growing up and being exposed only to the movie culture of the U.S., I didn't expect that. But one learns.

HATHAWAY: Again, your own attitude is--

HANNUN: We need to [stop].

HATHAWAY: We're going to-- This is going to be it, right?

HANNUN: I think so. How about you? [tape recorder off]

HATHAWAY: We were talking about the women in your lab and how you sensed that there were issues facing women, but that you wouldn't ascribe it to some sort of political consciousness on your part. That it's not much of an issue in your lab. And also, I think that was also the case for nonwhite, non-American people, as well, who-- And again, if you look at the list or the roster of your lab, that's the best indication that what you said is true. I think maybe it was more than 50 percent.

HANNUN: Oh, I don't know-- One, two, three, four, five. Well, I think now it's fifty-fifty. There were times when there were more women than men, for example. Maybe I didn't mention that, but I'm also sensitive because my wife is a professional woman, and she senses a lot of prejudice too. Again, it's something I don't sense. You know, it could be the same situation we're in at the same time, but she senses prejudice that I don't.

HATHAWAY: Now, prejudice against the both of you or against--?

HANNUN: No, against her as a woman.

HATHAWAY: Okay. As a woman. Is it something that you think you've become sensitized to, or is it still something you just don't pick up on? I mean, are you kind of, not doubting it, but just--? You seem to be taking it seriously, so—

HANNUN: I don't doubt her when she says that. I mean, sometimes I can sense it--maybe because I am sensitized to it--but many times I cannot sense it, which may be more subtle. Maybe I really shouldn't say that.

HATHAWAY: There's a common, I think, misperception among people that "I'm not racist or I'm not sexist because I feel I'm not." And they don't understand that actually whether one is or isn't something like that isn't so much how they feel about themselves but, of course, the perceptions of their actions and words as others perceive them.

HANNUN: Yeah. The one thing that I do-- There are many things that I think are not directed against women as such--prejudice against women--but against their level or the role they're assuming at any one time. And then it becomes a catch-22. For example, when I was a more junior faculty and would suggest something in a faculty meeting, it was as if I wasn't in the room. Now I can say a more stupid thing and everybody listens. (laughter] And I think also by keeping women sort of at a more junior level, they go through the same thing. That's why I'm describing it, because Lina, my wife, would say that, "I was in this meeting, and no one listens to me. They talk as if I wasn't in the room." And I don't know, is it because she's a woman or she's considered too junior? A lot of the prejudice women experience is maybe more because either they're in junior positions or because it's always assumed that they end up being the ones who compromise. Especially working married women with children. Is it they don't get paid as much because they're women, or is it they have to move with their spouse--the spouse got the best job and they have to compromise?

HATHAWAY: This is kind of a self-perpetuating—

HANNUN: The prejudice may be not more at the workplace as much as the prejudice arising more at the level of the family, that the woman is the one sacrificing other things for the sake of the family--the husband, the children, keeping the family together. Maybe if more men start sacrificing, they will start being this--

HATHAWAY: I was going to say, have you noticed--? Well, you've been in professional situations since, let's say, med school, so you've been around for a while. Maybe in Beirut it wasn't-- I mean, I take it there were women attending, though.

HANNUN: Yeah, yeah.

HATHAWAY: I mean, your wife is an example. Yeah, right, she was there. Maybe it's unfair to ask because you've spent so much time in a culture that you think is in more ways not so much sexist but the relationship or the role of women in that culture tends to not allow so much for a comparison with our culture, which is now supposedly not doing things like assigning roles according to gender and whatnot.

Another thing I wanted to ask you, because I think by far the majority of people I'll be interviewing are, well, I don't know, "white men" sounds almost kind of not nice--

HANNUN: Homegrown boys.

HATHAWAY: Okay. All Americans-- Caucasian males. There. I would like to take the opportunity with my interviewees who aren't to just ask if they have a sense of feeling like outsiders because of that. I also would like to ask you, because you've talked quite a bit at length about that sense you had as an outsider, not, again, being discriminated against so much, but growing up in Beirut as a non-Lebanese.

HANNUN: Well, I mean, in Lebanon I could sense that if I had to become a part of society, a productive rather than just in a student role, that would have opened a lot of discrimination. I could sense that. I don't think that exists to any comparable degree in the States. I'm still an outsider because most of my formative years were in a different culture altogether. I'm missing a lot of the cultural upbringing of other people in society. And there are many things not in my consciousness that are in the American consciousness. So that forces me to be an outsider. I come from, as I said, a culture where family ties are strong, where societal ties are strong. They're not in this country. It makes it obviously easier to make that switch than the reverse switch. You almost cannot penetrate in the reverse direction. So I do have that perspective of an outsider, and I always wonder what my children will grow up to be. I mean, they seem to be growing up more like totally American children, which is fine. I don't see any necessity for giving them the dilemmas and agonies we've been through in terms of cultural adaptation. Although they'll probably recognize their heritage and hopefully be proud of it. The other part of your question, I guess--

HATHAWAY: Well, is there a sense of--?

HANNUN: Discrimination? Is that something you--?

HATHAWAY: Or even just rude-- I mean, just a sense that sometimes you've come up against this situation. I'm also not unaware of the fact that here I am--a white Caucasian male--asking you this. I don't want you to think that I'm expecting you to just find that there is. And I hope that you're not offended that I'm asking the question.

HANNUN: No, not at all. Again, coming from the Middle East, the fact that I'm now an American citizen, with equal rights like anyone else, and treated almost I think the same as anyone else, with respect--definitely with respect for my role and my function--if there is a problem, it can't be of any serious magnitude. I have had the sense, very subtle sense at times, that had I been a white American boy I would have had maybe more doors opened to me, or opened a little easier, or people wouldn't be as apprehensive about what they're getting into.

HATHAWAY: How interesting.

HANNUN: And because I've sort of come to a more leadership position in academic medicine, that to me looks like an easily explained perspective. If we get an applicant to our program from either a foreign medical school or undergraduate] school, either applying for the medicine or for the graduate program-- You know, if you don't have a familiarity with the program, with the curriculum, with the degree of accomplishment, I'm sure that automatically translates into bias. I mean—

HATHAWAY: Or more, at a minimum, let's even say, it was just-- I mean, obviously you're suggesting you would do it too. If somebody's got a medical degree from maybe somewhere in Europe or something, automatically a flag goes up and you're going to give that--

HANNUN: Yeah. How are those people going to do in an American environment? I'm sure, therefore, that I was considered in that light too. I'm sure that I assumed that, when I was going through the system, I always--

Therefore, I assumed constantly that I always had to go the extra step before I can achieve or-- Well, I always performed the extra steps. Whether it was really needed or not, I do not know.

HATHAWAY: Maybe sometimes or maybe early-- I'm wondering now, though, if you were like sitting on a committee for even a senior position, let's say an associate or a full professor level here in your department-- You were on the committee, and a person whose name was clearly not American came across your desk. And let's say you had the name-- You know, something clicked in your mind, or you knew that name or had some reason that it stood out. And then you would kind of look through, and, indeed, the person went to a foreign medical school. But, you know, you have these lists of publications. They're in your situation. Would you kind of drop that flag? In other words, because they've already kind of gone through this process? I guess I'm asking about you now. Do you get a sense that you have as much opportunity as your colleagues?

HANNUN: Oh, yeah. I would not only drop the flag, but I mean I also many times play the advocate for people coming from either Third World countries or foreigners. Especially because I know that having had no opportunities to prove my abilities beyond just passing the courses, I appreciate the degree of achievement. So that's always been my point of view.

HATHAWAY: That they probably went the extra steps, like you did.

HANNUN: Yeah. If they're interested in coming to study hematology, that-- If they're interested in academic medicine but they have not done anything coming out of even some countries in Europe, it's probably they didn't have the opportunity. Actually, I'd generalize it even coming out of-- For some reason, someone stayed in x college of South Carolina or something, and now they've sort of been turned on to academics. I would give them the benefit of the doubt. I would be more hesitant, actually, about someone coming from Boston. Someone who grew up in Boston, has no academic achievement whatsoever, and now is coming to be considered for an academic position, either graduate school or fellowship or whatever, that's where actually now I raise the flag. Because someone who's had all those opportunities is the one that never exercised them, versus someone who's never had the opportunity but you can always tell that whenever they got even the slightest opportunity they grabbed it. So, no, I don't think I practice that kind of bias. I don't even mean bias, but what I said is I can see how the unknown translates into hesitation, and hesitation is obviously a minor degree of bias. And that's why I had always to sort of make sure that I went the extra step.

HATHAWAY: But, clearly, you've never had a sense that there is-- Certainly like it's political or there are discussions beyond your earshot or something about that-- Or the fact that you--

HANNUN: Yeah. Not at all. I mean, remember, I am in an academic situation.

HATHAWAY: And you kind of came into one-- One hopes that usually--

HANNUN: Yes, one hopes these things don't, you know-- I've been totally unaware of anything like that.

HATHAWAY: I was going to say, I think regions of the country and actually just traditions in schools, I think also, perhaps, public versus private situations-- There are differences, however. For instance, I think some places are more open to having women really finally climb way up the ladder and take equal positions with men. I remember interviewing somebody. We tried to come up with women who were like chairs of departments, ran institutes-- The way-out question being "When will a woman run the Whitehead [Institute] or something like that?" And we actually couldn't come up with very many at that time, but I've come up with a few more in just general reading. But what is the--? Maybe it's something you don't particularly give a lot of thought to, but Duke and its situation-- Would you say that there's a lot of women, and they have come up through the--? What do they say now, it's about half and half--Ph.D.'s? Since I don't know about M.D.'s-- Still like 20 percent?

HANNUN: No. Probably among M.D.'s the women are a much higher proportion.

HATHAWAY: Oh, really?

HANNUN: But, again, not in leadership positions. Yeah, Duke doesn't have many women in leadership positions. I would say very few.

HATHAWAY: Like nobody is chairing a department in the medical school or biological science.

HANNUN: No, no chairs. No.

HATHAWAY: Or running a lab or a lab with a name to it.

HANNUN: Yeah. There are a couple running labs.

HATHAWAY: I'm trying to think of a-- I was thinking like a lab that's got special funding, that may have lots of PI's [principal investigators] in it or something like that. Kind of like an institute within a--

HANNUN: Yeah, yeah. We don't have that, but we only have maybe one or two males that do that. See, I know there is a lot of bias against women in the community at large, but in academia I think the bias is not conscious bias. There is some of that, and you can see, like a faculty member, as I mentioned, being uncomfortable with women. You could tell that this is because of some problem. But most of the real bias is more subtle, and I really think it's because the successful "role model" in our society--and definitely in academia--is the more aggressive, what you keep mentioning, the eighty-hour-a-week person. And it seems to me that-- First of all, I think this is a myth that one has to work eighty hours a week to be successful.

HATHAWAY: Yeah. I'm exaggerating. I realize that too.

HANNUN: And I would sometimes question how successful someone can be if they need to work eighty hours a week.

HATHAWAY: And maybe the determination and aggressiveness part of what you're saying is

actually a more accurate way of talking about this kind of almost stereotyping the biology Ph.D.

HANNUN: That's what people look for when they want to choose a position of leadership, you know, a chairman and a director and whatnot. And that automatically selects against most women because most women with families cannot put all their energy into being aggressive about their jobs. It also selects against men who want to be committed to their families. Unless I was very lucky in setting up my operation and worked very hard on it, I can see that, if any one component of what I was doing fell apart, I wouldn't have moved to where I am now. So the whole system, in terms of moving on to lab operations, is selecting for people with a more aggressive capacity.

HATHAWAY: Do you think that's something that is okay? I mean that that's perhaps the way it will always be? Women will just have to become more aggressive or--?

HANNUN: Well, I think that's a price for wanting to get results. If you want the doers to do things-- You know, the doers are the achievers, the more aggressive people. If you want to solve the question of male-to-female ratios, you probably have to solve it as much at home and get it to a point where in half the households the female is the person primarily career active and the husband is the one compromising, and the other half vice versa. Then you'll have equal bias both ways. But to undo the requirement for aggressive, sort of male-type characteristics and leadership positions, that's talking about a major overhaul of the system. I mean, in terms of how can you get a very laid-back person, basically, as we say, to crack the whip and get things going, whether it's a department or a-- I don't know. I know it's doable. I know it's doable at the level of individual gifted people. But how do you get the whole system functioning--?

HATHAWAY: You know, perhaps there are men as well as women out there who are doing some big administrative or whatever sorts of jobs where they're coordinating the work of others and more so and kind of keeping it all together. And they're not really aggressive about it.

HANNUN: They're effective, but they're not aggressive.

HATHAWAY: They're kind of low-key.

HANNUN: Very effective. Usually they are the smarter people, the more self-confident people. But they're the exception. And they're going to stay as exceptions because it's a really formidable collection of traits to all put into one person. So I don't know. I mean, that's really getting into how do you overhaul the whole system. And I don't know.

HATHAWAY: No. And we don't want to go too much into what the future looks like beyond your own personal-- And that's, again, to just round this out-- I guess where I would go and what I'll ask you-- Maybe I'll put it in this way: What about yourself? Do you see yourself as striving toward running a department or running an institute? Or are you going to decide that, oh, after another five years, it's going to be your wife's turn to be the aggressive one and you're going to stay home with the kids a little more and maybe you'll just kind of be the laid-back type who does his own work? Or you just don't know?

HANNUN: The bottom line is I don't know. And actually, I had a discussion with my chairman last year, and he has good insight into that because he is a very effective chairman. He really--

HATHAWAY: And who is this?

HANNUN: This is Joe [Joseph C.] Greenfield. He's a chairman who takes pride in having people grow under him. Because if you look around, most chairmen--or many chairmen, many directors, many chiefs, whatever--they're much more out there to protect their own part of the operation. And actually, they can be envious of other people growing in the system. So our chairman is very effective from that point of view. What he said was--Because he's been through it. He was a researcher, then head of the division within a department, and then head of the department.

HATHAWAY: Okay. Now, he's the head of the Department of Medicine.

HANNUN: Medicine. Yeah.

HATHAWAY: Which is really the whole--?

HANNUN: That's the whole internal medicine. A few hundred, two or three hundred faculty.

HATHAWAY: It's huge.

HANNUN: It's the biggest department in the school of medicine.

HATHAWAY: Sounds like one of the biggest departments in the country.

HANNUN: It's probably as big as all the other departments put together. And he said, "You go through phases. Who knows what's the next phase? You may want ten years from now to say, 'I've had enough. I've got my intellectual stimulation from this. I want to enjoy now having other people grow under me. And, you know, take a more administrative job.'"

There is a problem with the system, the way I see it. In medicine, in academics, the rewards for doing a good job, whether it's in clinical medicine or in research, primarily are given out as administrative jobs. It's very weird. [laughter] I think it used to be okay when departments were real small. Out of a group of three, four, or five, one would become a chairman. So it was okay. But--

HATHAWAY: They were still obviously doing benchwork, probably.

HANNUN: Yeah. But when you talk about a department of a couple of hundred people, that's not okay.

HATHAWAY: You mean you're not interested in it at all?

HANNUN: At this point?

HATHAWAY: At this point.

HANNUN: Well, I mean the whole system is very-- The way the system rewards-- There are very few systems to allow people to grow and be rewarded by, let's say, staying in basic research. One probably would be the Howard Hughes [Medical Institute] and maybe a couple of-

HATHAWAY: That's rewards in the sense of just perhaps allowing your lab to expand, an infusion of money, and-

HANNUN: Expand, yeah, and grow.

HATHAWAY: Maybe better salaries. I mean, earn more so you can buy the boat or take the longer vacation.

HANNUN: And the security of being in Howard Hughes.

HATHAWAY: Sure. No more NIH applications if you don't want to.

HANNUN: I mean, how long can I stay--? What if my next grant gets in trouble for eight months? That would be a major disappointment. How long can I stay with--? They're minor at this point, but they could be more than minor anxieties and irritations and interruptions to my research. You know, there are endowed chairs here and there to do research. That's obviously one possibility for me. Administratively, I happen to be in a specialty in hematology/oncology in which to assume a leadership administrative position is almost a kiss of death for my research. I mean, our division has thirty-five faculty in hematology and medical oncology.

HATHAWAY: Right. You've become an administrator. mean, that's not bad for those who like to do that.

HANNUN: If I want to do it ten years from now, that may be fine. But it's not something I see myself doing now. So I don't know. Actually, the way my wife and I approached this career move when I first set up my lab here was to actually give it five years. That was back in '87, late '87. Give it five years and see what turns out with research. I mean, is it going to excite sufficiently to stay in or not? We've passed that sort of landmark or whatever.

HATHAWAY: Did you also kind of, at that point, in five years, sit down and--?

HANNUN: No. We're sort of now in a transition where we'd like to make some guidelines on what we would consider as a satisfying career maybe in the next five years or ten years.

HATHAWAY: Does that include maybe not being here but going elsewhere? Or it's more flexible than that?

HANNUN: More flexible. Define criteria. I mean, like we did the first time. There wasn't any rigorous criteria, but just are we going to evaluate what we have achieved as significant or not. It was as simple as that, in a way, and as difficult as that, in another way. You know, set up different criteria. I think my chairman is right. People evolve as they grow. Who knows, maybe five years from now I'll be bored with basic research, although I really don't see that.

HATHAWAY: And running a clinic in Central America, who knows.

HANNUN: Yeah. Ten or fifteen years from now, maybe I'll just find that I would be much more gratified if I do run a clinic in some Third World country, especially with my kids all grown up and all set on their own path. I don't know. But there is this discrepancy so I-- If the next level in-- Of course, you know, associate professor, the next level will be professor. You know, big deal. That's not materially any different. But that's about the limit of growth in what I'm doing now. And it's fine had it not been for the current NIH mess. I mean, really sort of doing research with a 10 percent or lower cutoff point is--

HATHAWAY: It's a risky business.

HANNUN: It makes it a risky business, and I don't see myself wanting to take that risk forever. I know now I'm in a good competitive position for my next round. But maybe next round I want to do something even quite crazy and quite innovative and scaled-down. I don't want to be really limited by this five-year cycle of 10 percent funding, where if you not only don't conform to the book but totally excel in every aspect, you feel like you're threatened. That could become a serious consideration. I would not want to be in that for a long time. Had it not been for that, one option definitely would be just to stay as I am and keep doing it until it really gets to be boring again or I become ineffective at it.

HATHAWAY: And I take it-- I almost don't think I'll ask the question except to kind of answer it myself. That is, if you look at the short term, you know, it's a matter of you've got young children and you've got an interesting job here and that's what you'll be doing.

HANNUN: Yeah. That's right.

HATHAWAY: Okay. I don't have anything else. You know, this is really it. I'm done. I think there's a lot of valuable and interesting and insightful information here. And I appreciate your time.

HANNUN: Oh, no problem.

HATHAWAY: And also the hospitality I find here.

HANNUN: No problem

[END OF TAPE 7, SIDE 2]

[END OF INTERVIEW]

INDEX

M

N

O

P

Q

R