CHEMICAL HERITAGE FOUNDATION

ADRIAN R. KRAINER

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Andrea R. Maestrejuan

at

Cold Spring Harbor Laboratory
Cold Spring Harbor, New York

on

9, 10, and 11 April 1997

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

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 © 1999, 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:

Holly Polish, Program Intern, Oral History, Chemical Heritage Foundation. B.A. History, American 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. B980808

This Interview Agreement is made and entered into this 6th day of August, 1998 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 ADRIAN R. KRAINER, having an address at P.O. Box 100, Cold Spring Harbor Laboratories, Cold Spring Harbor, New York, 11724, hereinafter called "Interviewee." This interview agreement supersedes any previous agreements regarding "the Work" described below.

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about April 9, 1997, and entitled "Interview with Adrian R. Krainer". 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. University agrees that portions of the Work, to be determined by Interviewee, will be sealed and will not be available for public access until January 1, 2050, or during the interviewee's lifetime, whichever is the earlier.

3. By virtue of the assignment specified in Article 1, University shall have the right to use the unsealed portions of the Work for any research, educational, or other purpose, including electronic reproduction, that University may deem appropriate At the end of the period specified in Article 2, University shall have the right to use the entire Work for any research, educational, or other purpose, including electronic reproduction, that University may deem appropriate.

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

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

6. 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.

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

If to University: Office of Research Administration
University of California, Los Angeles
P.O. Box 951406
Los Angeles, California 90095-1406

Attention: _____

If to Interviewee: Adrian R. Krainer
Cold Spring Harbor Laboratories
P.O. Box 100
Cold Spring Harbor, New York 11724

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

INTERVIEWEE

Adrian R. Krainer
(Signature)

Adrian R. Krainer
(Typed Name)

Cold Spring Harbor Laboratories
(Address)

P. O. Box 100

Cold Spring Harbor, NY 11724

Date 6-29-98

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

Patricia Brennan
(Signature)

Patricia Brennan, Director
for/Copyright Officer
UCLA-Sponsored Research
1400 Ueberroth Building
Box 951406
Los Angeles, CA 90095-1406

Date 8/6/98

Pew Scholars in the Biomedical Sciences

Chemical Heritage Foundation Internet Posting Release Form

I, Adrian R. Krainer, Ph.D., hereby request that my wishes be followed as per the checked selection below with regards to posting portions of the digital copy of the audio-taped interview of me and the related written transcript on the internet for non-commercial, educational use only.

Please check one:

a. _____ **No restrictions for Internet Posting.**
NOTE: Users citing this interview for purposes of publication are obliged under the terms of the Chemical Heritage Foundation Oral History Program to obtain permission from Chemical Heritage Foundation, Philadelphia, Pennsylvania.

b. _____ **Semi-restricted Internet Postings** (My review of the material intended to post is required.)

c. ✓ **Restricted access.** (Do not post.)

This constitutes my entire and complete understanding.

Adrian R. Krainer

Adrian R. Krainer, Ph.D.

6/27/08

Date

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

The Chemical Heritage Foundation (CHF) serves the community of the chemical and molecular sciences, and the wider public, by treasuring the past, educating the present, and inspiring the future. CHF maintains a world-class collection of materials that document the history and heritage of the chemical and molecular sciences, technologies, and industries; encourages research in CHF collections; and carries out a program of outreach and interpretation in order to advance an understanding of the role of the chemical and molecular sciences, technologies, and industries in shaping society.

ADRIAN R. KRAINER

1958 Born in Montevideo, Uruguay, on 14 September

Education

1981 B.A., Biochemistry, Columbia University
1986 Ph.D., Biochemistry, Harvard University

Professional Experience

Cold Spring Harbor Laboratory, Cold Spring Harbor, New York
1986-1989 Postdoctoral Researcher
1989-1990 Staff Investigator
1990-1994 Senior Staff Investigator
1994-present Senior Staff Scientist

State University of New York-Stony Brook, Stony Brook, New York
1990-present Faculty Member, Graduate Program in Genetics
1995-present Faculty Member, Molecular and Cellular Biology

Honors

1981 Phi Beta Kappa
1981 Phi Lambda Upsilon Honorary Chemical Society
1981 Josiah Macy Foundation Scholar
1986-1989 Cold Spring Harbor Outstanding Junior Fellow
1992-1996 Pew Scholar in the Biomedical Sciences

Selected Publications

Krainer, A.R. et al., 1984. Normal and mutant human E-globin pre-mRNAs are accurately and efficiently spliced in vitro. *Cell* 36:993-1005.
Krainer, A.R. andT. Maniatis, 1985. Multiplecomponents including the small nuclear ribonucleoproteinsUl and U2 are required for pre-mRNA splicing in vitro. *Cell* 42:725-36.
Krainer, A.R. et al., 1990. Purification and characterization of pre-mRNA splicing factor SF2 from HeLa cells. *Genes and Development* 4:1158-71.
Krainer, A.R. et al., 1990. The essential pre-mRNA splicing factor SF2 influences 5' splice site selection by activating proximal sites. *Cell* 62:35-42
Krainer, A.R. et al., 1991. Functional expression of cloned human splicing factor SF2: Homology to RNA binding proteins, Ul 70K, and *Drosophila* splicing regulators. *Cell*

66:383-94.
Mayeda, A. and A.R. Krainer, 1992. Regulation of alternative pre-mRNA splicing by hnRNP Al and splicing factor SF2. *Cell* 68:365-75.
Birney, E. et al., 1993. Analysis of the RNA-recognition motif and RS and RGG domains: Conservation in metazoan pre-mRNA splicing factors. *Nucleic Acids Research* 21:5803-16.
Caceres, J.F. et al., 1994. Regulation of alternative splicing in vivo by overexpression of antagonistic splicing factors. *Science* 265:1706-9.
Wu, Q. and A.R. Krainer, 1996. U1-mediated exon definition interactions between AT-AC and GT-AG introns of a Na+ channel gene. Science 274:1005-8.
Horowitz, D. and A.R. Krainer, 1997. Identification of a human homolog of yeast PRP18 and its role in catalytic step II of pre-mRNA splicing. *Genes and Development* 11:139-49.
Xu, R.M. et al. , 1997. Crystal structure of human UP1, the domain of HNRNP Al that contains two RNA-recognition mot ifs . *Structure* 5:559-70.

ABSTRACT

Adrian R. Krainer was born and raised in Montevideo, Uruguay in a Jewish family of eastern European descent (Hungary and Romania), the younger of two brothers. (Krainer's father was forced to work in a Romanian labor camp during World War II and on his way through Italy to Uruguay after the war, a clerical error changed the family name from Kreiner to Krainer). His parents had a small business making leather items in Montevideo. Political unrest framed his teenage years in the 1970s, as did the Zionist movement and witnessing anti-Semitism. Krainer went to a bilingual French elementary school (such that half of his classes were conducted in French, and half in Spanish) before transitioning into a public school for two years and then into a Hebrew school to complete his pre-college education. He was inspired by some of his high-school teachers to pursue science as a career, which he did instead of medicine, and developed an early interest in classical genetics. Seeing all the science being produced in the United States in genetics, Krainer decided that he wanted to attend a U.S. academic institution and set about learning English.

He applied to and decided to matriculate at Columbia University and major in biochemistry, finding a laboratory course with James A. Lewis and lectures by Charles R. Cantor quite stimulating. He worked for a time in a photocopying and messenger office on campus; he later worked in Catherine L. Squires's lab, successfully cloning a bacterial ribosomal operon. While still not feeling totally comfortable with the English language, he did quite well academically at Columbia, and was accepted both to Harvard University and the Massachusetts Institute of Technology's graduate programs, choosing the former for his doctoral research. While at Harvard, Krainer rotated through James Wang's and Walter Gilbert's labs, and wrote a computer program in Mathew S. Meselson's lab to correlate recombination frequencies and distance of residues within proteins, before joining the lab of Thomas P. Maniatis, who had done groundbreaking work cloning full-length cDNAs. While a graduate student, Krainer developed an efficient in vitro splicing system, which made it possible to study detailed aspects of human pre-mRNA splicing mechanisms, regulation, and disease-associated splicing defects. From this work Krainer had three articles published in *Cell*. He moved on to an independent fellow position at the Cold Spring Harbor Laboratory in Long Island, New York, being mentored by Richard J. Roberts (a co-discoverer of splicing in 1977) and worked on purifying and characterizing snRNP and protein components of the spliceosome, before accepting a faculty position there in 1989.

Throughout the interview Krainer talks about his scientific life and balancing family life with his career, all the while reflecting on life and science in Uruguay. In addition, he discusses Richard J. Roberts and Phillip A. Sharp's Nobel Prize; the system of staff promotion at Cold Spring Harbor; the rationale behind Cold Spring Harbor's "rolling-five system"; the National Cancer Institute grant review process; the advantages of the Pew scholars network; the growing tendency for clinical research to be funded over basic research; and James D. Watson' s program of bringing Eton students to Cold Spring Harbor. The interview ends with his thoughts on his participation in Programa de Desarrollo de Ciencias Básìcas and the Pew Latin American Fellows program; and the valuable interactions at the Pew scholars annual meetings.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Andrea R. Maestrejuan, Interviewer, UCLA Oral History Program; B.S., Biological Sciences , University of California, Irvine, 1986; M.A., History, University of California, Riverside, 1991; C. Phil., History, University of California, Riverside.

TIME AND SETTING OF INTERVIEW:

Place: Krainer's office, Cold Spring Harbor.

Dates, length of sessions: April 9, 1997 (132 minutes); April 10, 1997 (192); April 11, 1997 (215).

Total number of recorded hours: 9

Persons present during interview: Krainer and Maestrejuan.

CONDUCT OF INTERVIEW:

This interview is one ina 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 four-year Pew scholarships since 1988.

To provide an overall framework for project interviews, the director of the UCLA Oral History Program and three UCLA faculty project consultants developed a topic outline. In preparing for this interview, Maestrejuan held a telephone preinterview conversation with Krainer to obtain written background information (curriculum vitae, copies of published articles, etc.) and agree on an interviewing schedule. She also reviewed prior Pew scholars' interviews and the documentation in Krainer's file at the Pew Scholars Program office in San Francisco, including his proposal application, letters of recommendation, and reviews by Pew Scholars Program national advisory committee members. For technical background, Maestrejuan consulted J.D. Watson et al., *Molecular Biology of the Gene.* 4th ed. Menlo Park, CA: Benjamin/Cummings, 1987; Bruce Alberts et al., *Molecular Biology of the Cell.* 3d ed. New York: Garland, 1994; and Horace F. Judson, *The Eighth Day of Creation.* New York : Simon and Schuster, 1979.

The interview is organized chronologically, beginning with Krainer's childhood in Uruguay and continuing through his education at Columbia University, his graduate work at Harvard University, his postdoctoral work at Cold Spring Harbor Laboratory, and the establishment of his own lab at Cold Spring Harbor. Major topics discussed include Krainer's childhood in Uruguay, his work on in vitro splicing, crediting of authorship for publication, and the atmosphere and staffing structure at Cold Spring Harbor

ORIGINAL EDITING:

Gregory M . D . Beyrer, editorial assistant, 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.

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

Jane Collings, senior editor, prepared the table of contents and biographical summary. Beyrer assembled the interview history and index.

TABLE OF CONTENTS

INDEX

D

E

F

G

H