CHEMICAL HERITAGE FOUNDATION

ROBERT D. NICHOLLS

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Andrea R. Maestrejuan

at

Case Western Reserve University
Cleveland, Ohio

on

3, 4 and 5 September 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.

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. 970916

This Interview Agreement is made and entered into this 26th day of May, 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 ROBERT D. NICHOLLS, having an address at Department of Genetics, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, Ohio 44106-4955, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about September 3, 1997, and tentatively entitled "Interview with Robert D. Nicholls" 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 Research Administration
University of California, Los Angeles
P.O. Box 951406
Los Angeles, California 90095-1406

Attention: Ms. Carli V. Rogers
Copyright Officer

If to Interviewee:

Robert D. Nicholls
Department of Genetics
Case Western Reserve University
10900 Euclid Avenue
Cleveland, Ohio 44106-4955

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

INTERVIEWEE

Robert Nicholls
(Signature)

Robert D. Nicholls
(Typed Name)

Department of Genetics

Case Western Reserve University
(Address)

10900 Euclid Avenue

Cleveland, OH 44106-4955

Date 9-3-97

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

(Signature)

Carli V. Rogers
(Typed Name)

Copyright Officer
(Title)

Date 6/26/98

Chemical Heritage Foundation
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ROBERT D. NICHOLLS

1960 Born in Ballarat, Victoria, Australia, in March

Education

1980 B.Sc., University of Melbourne
1986 D.Phil., Oxford University

Professional Experience

Howard Hughes Medical Institute, Chevy Chase, Maryland
1987-1989 Research Fellow, Pediatrics

Department of Medicine and Mental Retardation Center/The Children's Hospital and Department of Pediatrics, Harvard Medical School, Boston, Massachusetts
1987-1989 Research Fellow

University of Florida College of Medicine, Gainesville, Florida
1990-1993 Assistant Professor, Departments of Neuroscience and Pediatrics
1993-1995 Courtesy Associate Professor

Case Western Reserve University and Center for Human Genetics, Cleveland, Ohio
1993-present Associate Professor, Department of Genetics

Honors

1989 Postdoctoral Clinical Research Award, American Society of Human Genetics
1990 Outstanding Achievement and Performance Award, State University System
1991-present Elected member, Human Genome Organisation
1990-1993 Basil O'Connor Fellow, March of Dimes Birth Defects Foundation
1991-1995 Pew Scholars Program in the Biomedical Sciences Grant

Selected Publications

Nicholls, R.D. et al., 1985. Recombination within the human embryonic xi-globin locus: A common chromosome produced by gene conversion of the psi xi gene. *Cell* 42:809-19.

Nicholls, R.D. et al., 1987. Recombination at the human alpha-globin gene cluster: Sequence features and topological constraints. *Cell* 49:369-78.

Nicholls, R.D. et al., 1989. Genetic imprinting suggested by maternal heterodisomy in non-deletion Prader-Willi syndrome. *Nature* 342:281-85.

Mascari, M.J. et al., 1992. The frequency of uniparental disomy in Prader-Willi syndrome: Implications for molecular diagnosis. *New England Journal of Medicine* 326:1599-1607.

Rinchik, E.M. et al., 1993. A gene for the mouse pin-eyed dilution locus and for human type II oculocutaneous albinism. *Nature* 361:72-76.

Buiting, K. et al., 1995. Inherited microdeletions in the Angelman and Prader-Willi syndromes define an imprinting center on human chromsome 15. *Nature Genetics* 9:395-400.

Saitoh, S. et al., 1996. Minimal definition of the imprinting center and fixation of a chromosome 15q11-q13 epigenotype by imprinting mutations. *Proceedings of the National Academy of Sciences USA* 93:7811-15.

Nicholls, R.D. et al., 1998. Imprinting in Prader-Willi and Angelman syndromes. *Trends in Genetics* 14:194-200.

Gabriel, J.M. et al., 1998. A model system to study genomic imprinting of human genes. *Proceedings of the National Academy of Sciences USA,* Resubmitted.

Ji, T. et al., 1998. The ancestral Prader-Willi/Angelman syndrome deletion breakpoint region gene encodes a giant protein implicated in protein trafficking and is mutated in *jdf2* mice with neuromuscular and spermiogenic abnormalities. *Cell* Resubmitted.

Gabriel, J.M. et al., 1998. A transgene insertion creating a heritable chromosome deletion mouse model of Prader-Willi and Angelman syndromes. Submitted.

Gray, T.A. et al., 1998. An imprinted, mammalian bicistronic transcript encodes two nuclear proteins. *Nature,* submitted.

ABSTRACT

Robert D. Nicholls was born in a small town near Melbourne, Australia, one of four children. His father was in the Forests Commission, so the family moved fairly often until Robert's parents divorced when he was a teenager, at which time Mrs. Nicholls and the children moved to Inverloch, a town near the ocean. Though they moved often, they stayed within Victoria, and all the towns they lived in were small. As a result, Nicholls grew up loving the countryside and animals. He and his brother collected and raised frogs and tortoises. Schools were of variable quality; his last year in high school turned out to have some very good teachers for his interests, already science and medicine. He attributes his interest in part also to his sister's illness, which kept her in hospital for six or seven years when she was a child.

Nicholls wanted to study science, particularly biology, and he chose the University of Melbourne as the best school in the area. He found that he needed new study habits; he also needed a new sport, as he had quit Australian football and cricket, so he took up running, which he pursues to this day. During his first three years his lab work consisted of doing programmed experiments; in his fourth—honors—year, for which he had to qualify, he did his first real lab work. He worked in Barrie Davidson's lab on tyrosine amino acid biosynthesis in *E. coli.* He wanted to go to England after his fourth year, but the school year was different, so he spent eight months working, first delivering auto parts and then tutoring biochemistry.

Nicholls won the Royal Commission fellowship to work in David Weatherall's department. He went to work in Douglas Higgs' lab to study genetic disease involving brain function; he had 18 papers before finishing his PhD. Finally settling on the genetics of retardation, in particular Prader-Willi and Angelman syndromes, he chose Harvard as the best place to continue. He accepted a postdoc in Samuel Latt's lab because Latt was working with humans, not mice. He found Harvard aggressively competitive; when Latt died unexpectedly Nicholls left for University of Florida. He met Jacqueline Kreutzer, his fiancée, there, but otherwise did not find the support he desired, and he has now arrived at Case Western University as an associate professor in genetics. His fiancée, a pediatric cardiologist, is in Boston, Massachusetts, which adds to the complications suffered by two-career couples.

Angelman and Prader-Willi syndromes are random and so not preventable. Nicholls, who is close to his patients and their families, hopes that since neurological diseases are not amenable to gene therapy, an understanding of molecular mechanisms will eventually be helpful in treatment if not prevention. He is working on the implications of imprinting, collaborating with Bernhard Horsthemke's lab. He continues to write grants, publish, and run.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Andrea R. Maestrejuan, Interviewer, UCLA Oral History Program; B.A., History, University of California, Irvine, 1988; B.S., Biological Sciences, University of California, Irvine, 1988; C.Phil., History, University of California, Riverside.

TIME AND SETTING OF INTERVIEW:

Place: Nicholls's office, Case Western University.

Dates, length of sessions: September 3, 1997 (118 minutes); September 4, 1997 (124) ; September 5, 1997 (150).

Total number of recorded hours: 6.55

Persons present during interview: Nicholls and Maestrejuan.

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 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 Nicholls to obtain written background information (curriculum vitae, copies of published articles, etc.) and to agree on an interviewing schedule. She also reviewed prior Pew scholars' interviews and the documentation in Nicholls '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 general background on the recent history of the biological sciences, Maestrejuan consulted J.D. Watson et al., *Molecular Biology of the Gene.* 4th ed. Menlo Park, CA: Benjamin/Cummings, 1987, and Bruce Alberts et al., *Molecular Biology of the Cell.* 3rd ed. New York: Garland.

The interview is organized chronologically, beginning with Nicholls's childhood and continuing through his undergraduate education at University of Melbourne, his graduate studies at Oxford University, his postdoc at Harvard Medical School, and the establishment of his own labs at University of Florida and Case Western University. Major topics discussed include the differences in scientific research in Australia, the United Kingdom, and the United States; genetic imprinting; Prader-Willi and Angelman syndromes; balancing career and personal life; and collaboration, competition, and funding in the sciences.

ORIGINAL EDITING:

Jin Ah Lee, editorial assistant, edited the interview. She 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. Lee assembled the biographical summary and interview history.

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

William Van Benschoten, editor, prepared the table of contents.

Ödül Bozkurt, editorial assistant, compiled the index.

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