CHEMICAL HERITAGE FOUNDATION

MIGUEL C. SEABRA

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Helene L. Cohen

at

Imperial College School of Medicine
London, England

on

11, 12, and 13 September 2000

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:

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. T0914000

This Interview Agreement is made and entered into this 14th day of September, 2000 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 MIGUEL C. SEABRA, having an address at Department of Molecular Genetics, Division of Basic Medical Sciences, Imperial College School of Medicine, Sir Alexander Fleming Building, London, SW6 2A2, United Kingdom, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about Septmber 11, 2000, and tentatively entitled "Interview with Miguel C. Seabra". 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, including electronic reproduction, 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: Oral History Program
University of California, Los Angeles
Box 951575
Los Angeles, California 90095-1575

Attention: Director

If to Interviewee: Miguel C. Seabra
Department of Molecular Genetics
Division of Basic Medical Sciences
Imperial College School of Medicine
Sir Alexander Fleming Building
London SW6 2A2, United Kingdom

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

INTERVIEWEE

X Miguel Seabra
(Signature)

Miguel C. Seabra
(Typed Name)

Imperial College School of
(Address)

Department of Molecular Genetics

London, SW6 2A2, United Kingdom

X Date 9/12/00

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

Dale E. Treleven
(Signature)

Dale E. Treleven
(Typed Name)

Director, Oral History Program
(Title)

Date 9/14/00

Pew Scholars in the Biomedical Sciences

Chemical Heritage Foundation Internet Posting Release Form

I, Miguel C. Seabra, M.D., 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. X **No restrictions for Internet Posting.**
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c. _____ **Restricted access.** (Do not post.)

This constitutes my entire and complete understanding.

Miguel Seabra

Miguel C. Seabra, M.D., Ph.D.

2008/02/11

Date

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

MIGUEL C. SEABRA

1962 Born in Lisbon, Portugal, on 1 June

Education

1986 M.D., New University of Lisbon Medical School
1992 Ph.D., Biochemistry and Molecular Biology, University of Texas Southwestern Medical Center

Professional Experience

New University of Lisbon Medical School
1985-1988 Teaching Assistant, Department of Biochemistry

University of Texas Southwestern Medical Center, Dallas, Texas
1988-1992 Student Research and Teaching Assistant, Departments of Biochemistry and Molecular Genetics
1992-1993 Research Fellow, Department of Molecular Genetics
1993-1994 Instructor, Department of Molecular Genetics
1994-1997 Assistant Professor, Department of Molecular Genetics

Imperial College School of Medicine, London, England
1997-1999 Senior Lecturer (Associate Professor), Molecular Genetics, Division of Biomedical Sciences
1999-present Professor and Department Head

Honors

1986-1988 Young Investigator Fellowship, National Institute for Scientific Research, Portugal
1988-1993 Fulbright Program Scholar
1995-1999 Pew Scholar in the Biomedical Sciences

Selected Publications

Reiss, Y. et al., 1990. Inhibition of purified $p21^{ras}$ farnesyl: Protein transferase by Cys-AAX tetrapeptides. *Cell* 62:81-88.

Seabra, M.C. et al., 1992. Purification of component A of *Rab* geranylgeranyl transferase:

Apparent identity with the choroideremia gene product. *Cell* 70:1049-57.
Seabra, M.C. et al., 1993. Retinal degeneration in choroideremia: Deficiency of *Rab* geranylgeranyl transferase. *Science* 259:377-81.
Seabra, M.C. et al., 1995. Deficient geranylgeranylation of *Ram*/*Rab* 27 in choroideremia. *Journal of Biological Chemistry* 270:24420-27.
Shen, F. and M.C. Seabra, 1996. Geranylgeranylation of *Rab* proteins: Formation of a complex between mongeranylgeranyl-*Rab* and *Rab* escort protein. *Journal of Biological Chemistry* 271:3692-98.
Seabra, M.C., 1996. Nucleotide dependence of *Rab* geranylgeranylation: *Rab* escort protein interacts preferentially with GDP-bound *Rab. Journal of Biological Chemistry* 271:14398-404.
MacDonald, I.M. et al., 1998. A practical diagnostic test for choroideremia. *Ophthalmology* 105:1637-40.
Anant, J.S. et al., 1998. Mechanism of *Rab*geranylgeranylation: Formation of the catalytic ternary complex. *Biochemistry (ACS)* 37:12559-68.
Zhang, H. et al., 2000. Crystal structure of *Rab* geranylgeranyl tranferase at 2.0 Å resolution. *Structure Fold Des* 8:241-51.
Pereira-Leal, J.B. and M.C. Seabra. The mammalian *Rab* family of small GTPases: definition of family and subfamily sequence motifs suggests a mechanism for functional specificity in the *Ras* superfamily. *Journal of Molecular Biology* 301:1077-87.
Stinchcombe, J.C. et al., 2001. *Rab* 27a is required for regulated secretion in cytotoxic T lymphocytes. *Journal of Cell Biology* 152:825-34.
Hume, A.N. et al., 2001. *Rab* 27a regulates the peripheral distribution of melanosomes in melanocytes. *Journal of Cell Biology* 152:795-808.

ABSTRACT

Miguel C. Seabra grew up in Lisbon, Portugal, one of three sons; his father was an ophthalmologist and his mother a kindergarten teacher. Seabra liked school and did well when school was in session. Political upheaval in Lisbon caused chaos in his school in his fifth-grade year, and Seabra's uncle, who had been a minister in a previous administration, was arrested. His academic interests in high school were in science and mathematics.

Seabra's parents had expectations for their children and their careers, and his father had a great influence on his decision to enter medical school. While at medical school he worked under Fernanda Mesquita and had an internship in Turin, Italy. During his travels under the aegis of the Children's International Summer Villages he met the woman who became his wife, Isabel Fernandes Pinto. Soon after, he made the decision to seek a Ph.D. outside of Portugal and was accepted into the doctoral program at University of Texas Southwestern Medical Center in Dallas, Texas. His family was resistant to his moving to the United States; he had trouble, at first, with lectures in English; and he and his wife suffered quite a bit of culture shock and homesickness for a little while.

Seabra was directed by Scott Grundy to Joseph Goldstein's lab, where he continued his research on cell cholesterol metabolism with Michael Briggs and Yuval Reiss and helped purify the geranylgeranyltransferase enzyme, though he chose not to write his PhD thesis on geranylgeranylation; during his graduate work Seabra published a paper on *Rab* escort proteins in *Cell*. Ultimately he transitioned to a postdoc and principal investigator position at University of Texas Southwestern, working hard to overcome challenges when setting up his own lab.

After spending some time in his faculty position, Seabra decided to pursue his science abroad, moving to the Imperial College School of Medicine in London, England, for reasons that included funding growth in England, especially by the Wellcome Foundation; his wife's profession; and the language and culture. Core to his growth and development in the United States, however, was his receipt of the Pew Scholars Program in the Biomedical Sciences award, a topic that he talked about at length in the interview.

The interview concluded with Seabra's discussion of a typical workday, a workday that has made balancing family and career a challenge. He has had little time for working at the bench, much less for leisure activities. Experiencing firsthand the extreme competitiveness that exists in the global scientific community affected his beliefs and practices about science.

The interview ends with Seabra's opinions about ethics in science; the inevitability of scientific progress; and the impact of fashionable trends on the publication of scientific articles. He compares scientific collaboration in the United States and England, and explains his current research on prenylation of *Rab* proteins and possible applications of his research. He talks about the support he has received to cure choroideremia, and finishes with an elaboration of his personal and professional goals, an assessment of his achievements, and final thoughts on foregoing a possible Howard Hughes Medical Institute award.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Helene L. Cohen, Interviewer, UCLA Oral History Program. B.S., Nursing, UCLA; P.N.P., University of California, San Diego/UCLA; M.A., Theater, San Diego State University.

TIME AND SETTING OF INTERVIEW:

Place: Seabra's office, Imperial College School of Medicine, London, England.

Dates, length of sessions: September 11, 2000 (117 minutes); September 12, 2000 (140); September 13, 2000 (151).

Total number of recorded hours: 6.8

Persons present during interview: Seabra and Cohen.

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, Cohen held a telephone preinterview conversation with Seabra 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 Seabra'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, Cohen consulted J.D. Watson et al., *Molecular Biology of the Gene.* 4th ed. Menlo Park, California: Benjamin/Cummings, 1987; Bruce Alberts et al., *Molecular Biology of the Cell.* 3rd ed. New York: Garland, 1994; Horace F. Judson, *The Eighth Day of Creation.* New York: Simon and Schuster, 1979; and recent issues of *Science* and *Nature.*

The interview is organized chronologically, beginning with Seabra's childhood in Lisbon, Portugal, and continuing through his graduate work at the New University of Lisbon Medical School and the University of Texas Southwestern Medical Center at Dallas, and the establishment of his own lab at the Southwestern Medical Center at Dallas and, later, at Imperial College School of Medicine, London. Major topics discussed include his childhood and education in Portugal, his research in the Joseph L. Goldstein lab, and his research and teaching at the Imperial College School of Medicine.

ORIGINAL EDITING:

Deborah Kolosova, 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.

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

William Van Benschoten, editor, prepared the table of contents. Deborah Kolosova assembled the biographical summary and interview history. Ann Marie Davis, editorial assistant, compiled the index.

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