CHEMICAL HERITAGE FOUNDATION

JONATHAN M. HOROWITZ

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Andrea R. Maestrejuan

at

North Carolina State University at Raleigh
Raleigh, North Carolina

on

13-15 January 1998

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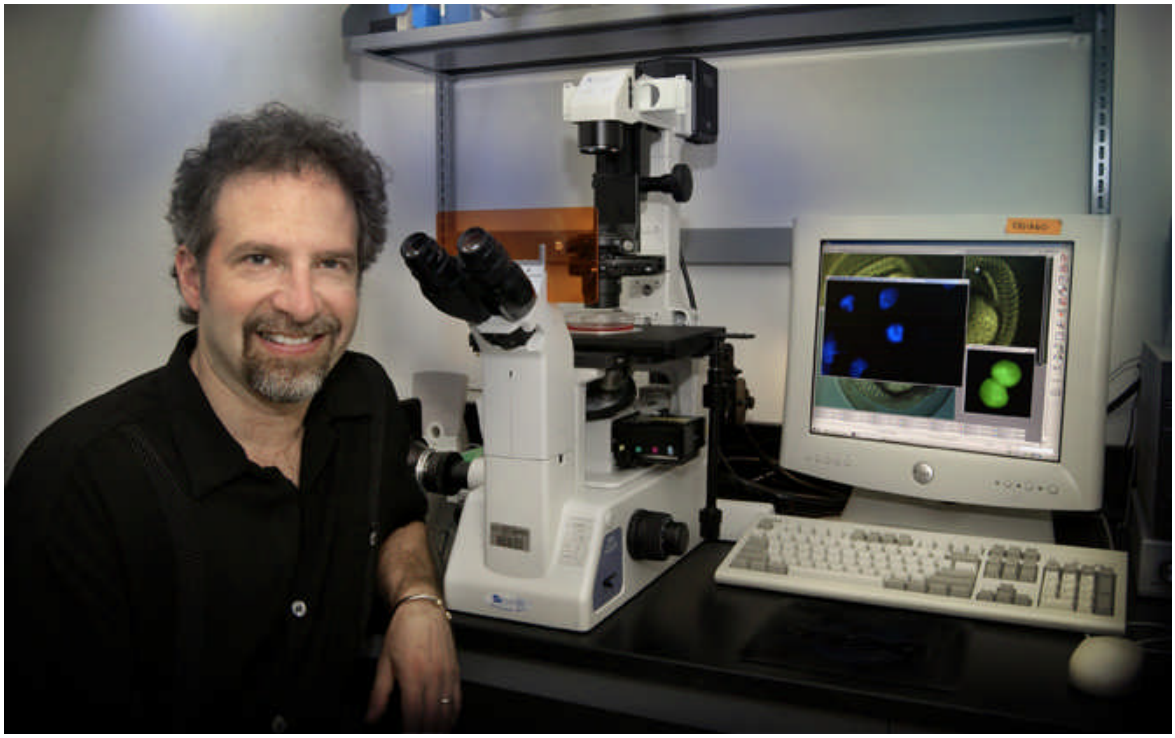

Jonathan M. Horowitz

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 the Pew Scholars Program in the Biomedical Sciences Advisory Committee members.

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REFORMATTING:

Marnie Berkowitz, Consultant to the Chemical Heritage Foundation. B.A., Classical Languages and Literatures, University of Minnesota; Ford Foundation Fellowship, Classical Languages and Literatures, University of Chicago.

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

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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 JONATHAN M. HOROWITZ, having an address at Department of Anatomy, Physiology and Radiology, North Carolina State University, College of Veterinary Medicine, Raleigh, North Carolina 27606, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about January 13, 1998, and tentatively entitled "Interview with Jonathan M. Horowitz". 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.

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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:

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If to Interviewee:

Jonathan M. Horowitz
North Carolina State University
College of Veterinary Medicine
Department of Anatomy, Physiology and Radiology
Raleigh, North Carolina 27606

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

NTERVIEWEE

J.M. Horowitz
(Signature)

Jonathan M. Horowitz
(Typed Name)

North Carolina State University

College of Veterinary Medicine
(Address)

Raleigh, North Carolina 27606

Date January 13, 1998

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

(Signature)

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Date 5/26/98

Pew Scholars in the Biomedical Sciences

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JM Horowitz

Jonathan M. Horowitz, Ph.D.

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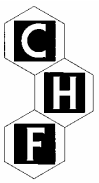

JONATHAN M. HOROWITZ

1958 Born in Brooklyn, New York on 24 June

Education

1980 B.A., Brown University
1985 Ph.D., University of Wisconsin-Madison

Professional Experience

Whitehead Institute for Biomedical Research
1986-1989 Postdoctoral Fellow

Brown University
1987 Adjunct Assistant Professor

Duke University
1989-1993 Assistant Professor, Section of Cell Growth, Regulation, and Oncogenesis
1989-1997 Assistant Professor, Department of Microbiology
1993-1997 Assistant Professor, Department of Molecular Cancer Biology

North Carolina State University at Raleigh, College of Veterinary Medicine
1997-present Research Associate Professor of Oncology, Department of Anatomy, Physiological Sciences, and Radiology

Honors

1991-1993 American Cancer Society Junior Faculty Research Award
1992-1996 Pew Scholar in the Biomedical Sciences
1994-1999 American Cancer Society Faculty Research Award

Selected Publications

Horowitz, J.M. and R. Risser, 1982. A locus that enhances the induction of endogenous ecotropic murine leukemia viruses in RF/J mice. *Journal of Virology* 44:950-57.

Horowitz, J.M. et al., 1985. Molecular and biological characterization of the endogenous ecotropic virus of BALB/C mice. *Journal of Virology* 56:798-806.

Horowitz, J.M. et al., 1987. Germ line integration of a murine leukemia provirus into a retrovirus-like sequence. *Journal of Virology* 61:701-7.

Friend, S.H. et al., 1987. Deletion of a DNA sequence in retinoblastomas and mesenchymal tumors: Organization of the sequence and its encoded protein. *Proceedings of the National Academy of Sciences USA* 84:9059-63.

Whyte, P. et al., 1988. Association between an oncogene and an anti-oncogene: The adenovirus E1A proteins bind to the retinoblastoma gene product. *Nature* 334:124-29.

Horowitz, J.M. et al., 1989. Point mutational inactivation of the Rb antioncogene. *Science* 243:937-40.

Horowitz, J.M. et al., 1990. Frequent inactivation of the retinoblastoma antioncogene is restricted to a subset of human tumor cells. *Proceedings of the National Academy of Sciences USA* 87:2775-79.

Robbins, P.D. et al., 1990. The retinoblastoma susceptibility gene product negatively regulates human c-*fos* expression and AP-1 transcriptional activity. *Nature* 346:668-71.

Chellappan, S.P. et al., 1991. The E2F transcription factor is a cellular target for the Rb protein. *Cell* 65:1053-61.

Udvadia, A.J. et al., 1993. Sp-1 binds promoter elements regulated by the Rb protein and Sp-1-mediated transcription is stimulated by Rb co-expression. *Proceedings of the National Academy of Sciences USA* 90:3265-69.

Sterner, J.M. et al., 1995. Detection of a novel cell-cycle regulated kinase activity that associates M with the amino-terminus of the retinoblastoma (Rb) protein in G2/M phases. *Journal of Biological Chemistry* 270:9281-88.

Rogers, K.T. et al., 1996. Identification and characterization of DP-2 proteins expressed *in vivo. Proceedings of the National Academy of Sciences USA* 93:7594-99.

Kennett, S.B. et al., 1997. Sp3 encodes multiple proteins that differ in their capacity to stimulate or repress transcription. *Nucleic Acids Research* 25:3110-17.

Tao, Y. et al., 1997. Subunit composition determines E2F-binding site specificity. *Molecular Cell Biology* 17:6994-7007.

Sterner, J.M. et al., 1998. Negative regulation of DNA replication by the retinoblastoma protein is mediated by its association with MCM7. *Molecular Cell Biology* 18: 2748-57.

ABSTRACT

Jonathan M. Horowitz was born in Brooklyn, New York. His father was a food photographer and his mother a housewife who later returned to work for a foundation. His family was "culturally" Jewish; their holidays were celebrated mostly with food rather than religious ceremonies. From an early age Horowitz was interested in science, particularly in "small things"; by high school age he had decided to obtain a Ph.D. and become a researcher in molecular biology, à la Francis Crick. He attended a new—and at that time trendy—high school where there were no competition, no sports, no grades; there he even designed his own courses.

Following what he describes as a "common theme" in his life, namely no planning, he decided to go to Brown University because someone he knew was a student there. She told Horowitz that Brown was unstructured, so he could skip classwork and just do research in a lab. At Brown, having to take classes after all, he struggled during his first year and was given a last chance to do well. He did finish, but with a poor grade point average. During his last year he took an ultrastructure class, in which he worked with Lloyd Matsumoto, an electron microscopy expert in Peter Shank's lab. Horowitz says that his main accomplishment in that lab was to have met his future wife, who was working there as a technician.

For graduate school, Horowitz was accepted at University of Wisconsin and at Johns Hopkins University. Not having investigated very much, he "asked around" as to which school he should attend. The brother of someone down the hall from Horowitz's lab ran a lab at Wisconsin, so Horowitz decided to go to Wisconsin. There he began with a rotation with Howard Temin; the rotation did not work out well, so Horowitz went to Rex Risser's lab to work on mouse retroviruses, notably strains of leukemia.

When his wife accepted a job at Harvard, Horowitz had to find a postdoc in the Boston area. Shifting his interest from retroviruses to oncogenes, he again "asked around" and was referred to Robert Weinberg's lab at the Whitehead Institute for Biomedical Research. Originally working on *ras* protein, he eventually switched to *Rb*, sequencing the *Rb* gene and trying to develop antibodies against it. In collaboration with Edward Harlow Horowitz discovered that *Rb* is an E1A-binding protein and mapped the E1A- binding region on *Rb*.

Finishing their postdocs, Horowitz and his wife had to find a place where both could have jobs. Horowitz's wife found a position at North Carolina State College of Veterinary Medicine, and Horowitz accepted an assistant professorship at Duke University. There he spent much of his time seeking support for his research. Duke's commitment to cancer research was hardly unwavering, and Horowitz's identity as a molecular cancer biologist counted against him in the tenure decision. When he was not granted tenure he accepted an associate professorship at North Carolina State College of Veterinary Medicine; here he finds much more support for his research, though he is still establishing his lab. He continues to work with the *Rb* gene; to seek funding; to publish; and to balance his work with his wife and two children.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Andrea 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: Horowitz's office, North Carolina State University at Raleigh.

Dates, length of sessions: January 13, 1998 (110 minutes); January 14, 1988 (122); January 15, 1988 (127).

Total number of recorded hours: 6.0

Persons present during interview: Horowitz 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' 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 Horowitz 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 Horowitz'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 and Bruce Alberts et al., *Molecular Biology of the Cell.* 3d ed. New York: Garland.

The interview is organized chronologically, beginning with Horowitz's childhood and education in Brooklyn and continuing through his work at Brown University, his graduate career at University of Wisconsin-Madison, and the establishment of his lab at Duke University and, later, at North Carolina State University. Major topics discussed include Horowitz's work on the *Rb* protein, involvement in the establishment of the Department of Molecular Cancer Biology at Duke University, and the current status of science funding in the United States.

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.

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

William Van Benschoten, editor, prepared the table of contents, biographical summary, and interview history. Ödül Bozkurt, editorial assistant, prepared the index.

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