CHEMICAL HERITAGE FOUNDATION

JOHN H. WEISS

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Andrea R. Maestrejuan

at

Costa Mesa, California

on

2, 3, and 4 October 1996

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. R120902C

This Interview Agreement is made and entered into this 9 day of December 2002 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 JOHN H. WEISS, having an address at University of California, Irvine, Gillespie Neuroscience Research Facility, Irvine, California 92697-4292, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about October 2, 1996, and tentatively entitled "Interview with John H. Weiss. 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:

Oral History Program
University of California, Los Angeles
Box 951575
Los Angeles, California 90095-1575

Attention: Janice L. Reiff

If to Interviewee:

John H. Weiss
University of California, Irvine
Gillespie Neuroscience Research Facility
Irvine, California 92697-4292

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

INTERVIEWEE

X _____
(Signature)

John H. Weiss
(Typed Name)

University of California, Irvine
(Address)

Gillespie Neuroscience Research Facility

Irvine, California 92697-4292

X Date 12/4/02

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

_____
(Signature)

Janice L. Reiff
(Typed Name)

Interim Director, Oral History Program
(Title)

Date 9 Dec 2002

Pew Scholars in the Biomedical Sciences

Chemical Heritage Foundation Internet Posting Release Form

I, John H. Weiss, 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:

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

This constitutes my entire and complete understanding.

John W Weiss

John H. Weiss, M.D., Ph.D.

2/5/08

Date

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

JOHN H. WEISS

1956 Born in San Francisco, California, on 5 June

Education

1979 B.S., Biology, Stanford University
1979 M.S., Biology, Stanford University
1983 M.D., Stanford University
1991 Ph.D., Neuroscience, Stanford University

Professional Experience

Stanford University Hospital, Palo Alto, California
1983-1984 Intern, Medicine
1984-1987 Resident, Neurology
1987-1991 Postdoctoral Fellow, Department of Neurology

University of California, Irvine
1991-1996 Assistant Professor, Department of Neurology
1992-present Staff Member, Medical Center
1996-present Associate Professor, Department of Neurology
1996-present Associate Professor, Department of Anatomy and Neurobiology and Department of Psychobiology

Honors

1980-1981 Stanford Medical Alumni Scholar
1980-1981 March of Dimes Medical Student Research Fellowship
1987-1990 American Academy of Neurobiology Research Fellowship in Neuropharmacology
1990-1991 Dana Fellow in Neuroscience
1990-1995 National Institute on Aging Clinician Investigator Award
1992-1996 Pew Scholar in the Biomedical Sciences

Selected Publications

Weiss, J. et al., 1986. Ketamine protects cultured neocortical neurons from hypoxic injury. *Brain Research* 380:186-90.

Weiss, J.H., and D.W. Choi, 1988. Beta-N-methylamino-L-alanine neurotoxicity requires bicarbonate as a cofactor. *Science* 241:973-75.
Weiss, J.H. et al., 1989. Bicarbonate dependence of glutamate receptor activation by beta-N-methylamino-L-alanine: Channel recording and study with related compounds. *Neuron* 3:321-26.
Weiss, J.H. et al., 1989. Neurotoxicity of beta-N-methylamino-L-alanine (BMAA) and beta-N-oxalylamino-L-alanine (BOAA) on cultured cortical neurons. *Brain Research* 497:64-71.
Weiss, J.H. et al., 1990. Cortical neurons containing somatostatin or parvalbumin-like immunoreactivity are atypically vulnerable to excitotoxic injury *in vitro. Neurology* 40:1288-92.
Weiss, J.H. et al., 1990. The calcium channel blocker nifedipine attenuates slow excitatory amino acid neurotoxicity. *Science* 247:1474-77.
Weiss, J.H. et al., 1994. Ca2 + channel blockers attenuate E-amyloid peptide toxicity to cortical neurons in culture. *Journal of Neurochemistry* 62:372-75.
Weiss, J.H. et al., 1994. Basal forebrain cholinergtic neurons are selectively vulnerable to AMPA/kainate receptor-mediated neurotoxicity. *Neuroscience* 60:659-64.
Turetsky, D.M. et al., 1994. Cortical neurons exhibiting kainate-activated Co2 + uptake are selectively vulnerable to AMPA/kainate receptor-mediated toxicity. *Neurobiology of Disease* 1:101-10.
Yin, H.Z. et al., 1994. Cortical neurons with Ca2 + permeable AMPA/kainate channels display distinct receptor immunoreactivity and are GABAergic. *Neurobiology of Disease* 1:43-49.
Yin, H.Z. et al., 1995. Zn^{2+} permeates Ca^{2+} permeable AMPA/kainate channels and triggers selective neural injury. *NeuroReport* 6:2553-56.
Carriedo, S.G. et al., 1996. Motor neurons are selectively vulnerable to AMPA/kainate receptor-mediated injury *in vitro. Journal of Neuroscience* 16:4069-79.
Ha, D.H. et al., 1996. Basal forebrain cholinergic neurons that contact cortical cells in culture display enhanced morphological features and decreased dependence on nerve growth factor. *Journal of Comparative Neurology* 373 :451-65.
Lu, Y.M. et al., 1996. Ca^{2+}-permeable AMPA/kainate and NMDA channels: High rate of CA^{2+} influx underlies potent induction of injury. *Journal of Neuroscience* 16:5457-65.

ABSTRACT

John H. Weiss grew up in San Francisco, California, the oldest of three children. His parents were both psychiatrists. He attended a private grade school and a less traditional high school; he found school interesting but not especially difficult. He developed his interest in math and science early, and he found that science came naturally to him as he was interested in discerning patterns in the way the world works.

Weiss entered Stanford University, where he majored in biology with a focus on neuroscience. After taking an extra year of undergraduate study, he applied to medical school. He spent six months in a biochemistry research lab, and he attended science classes while at Stanford University School of Medicine, but uncertainty prevented Weiss from seeking a lab position. He found that the practical challenges of medical residency proved more difficult than course work when he started a neurology residency. During that residency he met Dennis W. Choi and entered the Stanford Ph.D. program in neuroscience. In the Choi lab he began work on mechanisms of nerve cell degeneration in stroke and on glutamate's toxic effect on nerve cells. Choi proposed two phases of glutamate injury.

Research on nerve degenerative diseases on Guam led Weiss to study ß-N-methylamino-L-alanine (BMAA). His work in the Choi lab on BMAA yielded clues regarding AMPA/kainate receptor activation in nerve-degenerative diseases. He discovered that BMAA's toxicity depends on a covalent interaction with other compounds, explaining about AMPA/kainate toxicity and receptor activation, the role of voltage-sensitive calcium channels, BMAA's role in nerve-degenerative disease, and the finding that zinc accumulation in voltage-sensitive calcium channels might cause cell death (apoptosis).

Weiss accepted a position at University of California, Irvine, and received a Pew Scholars Program in the Biomedical Sciences award and a National Institutes of Health grant, though he did not have lab space immediately available at Irvine. While starting his lab he had teaching and clinical responsibilities, he had to find and hire postdocs, and he had to mentor students.

At the end of the interview Weiss discusses AMPA/kainate-type glutamate receptor-mediated toxicity in selective nerve cell degeneration; calcium in selective injury; a collaboration with the Choi lab to study “cobalt positive” NADPH-diaphorase cells; attempts to improve upon historically poor results of calcium imaging studies; correlating calcium influx and intercellular calcium levels with cell death; and the role of zinc in selective injury. His collaboration with Carl Cotman on ß-amyloid protein's toxicity in cortical cell cultures and new directions for research on cellular functions constituted his attempts to establish a reputation separate from Choi’s and to overcome the competitive pressure he felt in his field. He concludes by saying that he has found a supportive community at the Pew Scholars Program in the Biomedical Sciences annual meetings.

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: Weiss's home, Costa Mesa, California.

Dates, length of sessions: October 2, 1996 (116 minutes); October 3, 1996 (164) ; October 4, 1996 (81).

Total number of recorded hours: 6

Persons present during interview: Weiss 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 Weiss 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 Weiss'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 Weiss's childhood in San Franciscoand continuing through his education and postdoctoral work at Stanford University and the establishment of his lab at the University of California, Irvine. Major topics discussed include the question of how to conduct independent basic research in an applied science environment, Weiss's social conscience, and his work on nerve-cell degenerative diseases.

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.

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

Jane Collings, editor, prepared the table of contents and interview history. Beyrer assembled the biographical summary. Jin Ah Lee, editorial assistant, compiled the index.

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