CHEMICAL HERITAGE FOUNDATION

CHRISTINE E. HOLT

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Steven J. Novak

at

University of California, San Diego
San Diego, California

on

25, 26, and 27 October 1995

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

Christine E. Holt

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. R951102

This Interview Agreement is made and entered into this 5th day of February, 1996 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 CHRISTINE E. HOLT having an address at University of California, San Diego, Department of Biology, 0322, La Jolla, California, 92093-0322, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about October 25, 1995, and tentatively entitled "Interview with Christine E. Holt". 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 her 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, except for commercial applications.

3. Interviewee acknowledges that she will receive no remuneration or compensation for her 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: Ms. Carli V. Rogers
Copyright Officer

If to Interviewee: Christine E. Holt
University of California, San Diego
Department of Biology, 0322
La Jolla, California 92093-0322

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

INTERVIEWEE

Christine Holt
(Signature)

Christine E. Holt
(Typed Name)

University of California
San Diego

Department of Biology, 0322
(Address)

La Jolla, CA 92093-0322

Date 25 Oct 95

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

Carli V. Rogers
(Signature)

Carli V. Rogers
(Typed Name)

Copyright Officer
(Title)

Date 7 Nov 8, 1995

Chemical Heritage Foundation
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CHRISTINE E. HOLT

1954 Born in Wylam, England, on 28 August

Education

1977 B.Sc., University of Sussex
1982 Ph.D., Kings College, University of London

Professional Experience

University of California, San Diego, San Diego, California
1982 Postdoctoral fellow, Department of Biology
1984-1985 Postdoctoral fellow, Department of Biology
1985-1989 Assistant Research Biologist and Lecturer
1989-1992 Assistant Professor-in-Residence
1992-present Assistant Professor

Oxford University, Oxford, England
1983 Postdoctoral fellow, Department of Physiology

Max-Planck-Institut für Entwicklungsbiologie, Tübingen, Germany
1986-1987 Visiting Alexander von Humboldt Fellow

Wellcome Cancer Research Campaign Institute, Cambridge, England
1993-1994 Visiting scholar

Honors

1977-1980 Graduate fellowship, Science Research Council
1983 Junior Research Fellowship, Worcester College, Oxford University
1983 Training fellowship, Medical Research Council
1986-1989 McKnight Scholars Award for Neuroscience
1991-1994 Pew Scholar in the Biomedical Sciences

Selected Publications

Holt, C.E., 1980. Cell movements in *Xenopus* eye development. *Nature,* 287:850-52.
Holt, C.E. and W.A. Harris, 1983. Order in the initial retinotectal map in *Xenopus:* A new

technique for labelling growing nerve fibers. *Nature,* 301:150-52.
Holt, C.E., 1984. Does timing of axon outgrowth influence initial retinotectal topography in *Xenopus? Journal of Neuroscience,* 4:1130-52.
Harris, W.A. et al., 1987. Retinal axons with and without their somata, growing to and arborizing in the tectum of *Xenopus* embryos: A time-lapse video study of single fibers *in vivo. Development,* 101:121-33.
Holt, C.E. et al., 1988. Cellular determination in the *Xenopus* retina is independent of lineage and birth date. *Neuron,* 1:15-26.
Thompson, I.D. and C.E. Holt, 1989. Absence of activity inhibits clustering of retinal terminals in the ipsilateral superior colliculus of neonatal hamsters. *Journal of Comprehensive Neurology,* 282:371-88.
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Cornel, E. and C.E. Holt, 1992. Precocious pathfinding: Retinal axons can navigate in an axonless brain. *Neuron,* 9:1001-11.
Chien, C-B. et al., 1993. Navigational errors made by growth cones without filopodia in the embryonic *Xenopus* brain. *Neuron,* 11:237-51.
Lilienbaum, A. et al., 1995. Chimeric integrins expressed in retinal ganglion cells impair process outgrowth *in vivo. Molecular and Cellular Neuroscience,* 6:139-52.
Chien, C-B. et al., 1995. Absence of topography in precociously innervated tecta. *Development,* 121:2621-31.
McFarlane, S. et al., 1995. FGF signaling and target recognition in the developing visual system. *Neuron,* 15:1017-28.
Worley, T. and C.E. Holt, 1996. Inhibition of protein tyrosine kinases impairs axon extension in the embryonic optic tract. *Journal of Neuroscience,* 16:2294-306.

ABSTRACT

Christine E. Holt was born and raised in Wylam, a small village in Northumberland in the north of England, the youngest of three siblings. Her mother was a homemaker; her father was a naval sea captain during World War II, who then worked in the safe business and then the shipping business. She enjoyed exploring nature surrounding her home with her older brother, spending some time badger-watching, and she also played the piano. She attended British public schools (the equivalent of American private schools), and at the age of ten she was enrolled in a boarding school in which she stayed until she was sixteen. She enjoyed sports, including rounders and netball, and in school she split her focus between literature and the arts, and biology, but not other sciences; she had an interest in anthropology as well that was heightened by two trips to Africa during summer holidays. Holt's biology teacher at her college preparatory school taught with an outdated syllabus and so Holt decided to teach herself biology using Michael B.V. Roberts's textbook, *Biology: A Functional Approach*.

She matriculated at the University of Newcastle upon Tyne to study zoology but then transferred to the University of Sussex, where she had opportunities to talk directly with professors like John Maynard Smith and was under the tutelage of Michael F. Land who encouraged her to undertake graduate studies. She received a very competitive Science Research Council fellowship for her doctoral studies and chose to work with John H. Scholes at the Medical Research Council (MRC) Cell Biophysics Unit in an attempt to unify her interests in genetics and neurobiology. At the MRC Holt faced challenges establishing *Xenopus* lines, though she was able to use radioactively-labeled amino acids to trace axon development. William A. Harris introduced her to the concept of using an electrophysiological mapping system with *Xenopus*, after which she decided to undertake her postdoctoral studies with him at the University of California, San Diego (and, subsequently, they married). Her research focus in Harris's lab was, predominantly, disproving the mechanospatial theory of brain development and contributing to the reaffirmation of Roger W. Sperry's chemoaffinity theory, which argued that every cell in the retina was specified with a different tag that matched a complementary tag in the tectum. From there she went on to another fellowship with Colin Blakemore at Oxford University to study mammalian cell development, through which she realized the impracticality of using hamsters to investigate early brain development and also the inability to demonstrate axon—tectum chemoaffinity in chicken culture. She then returned to San Diego as a researcher and, later, a professor. Soon after her fellowships and her return to San Diego, Holt and Harris spent a sabbatical with Friedrich Bonhoeffer at the Max-Plank-Institut für Entwicklungsbiologie in Tübingen, Germany, where Holt used time-lapsed video to observe *Xenopus* retinal axon *in vivo* and she investigated the possibility of guidepost cells in brain development. Soon after her return to San Diego, Holt received the Pew Scholars Program in the Biomedical Sciences award, with which she worked on developing the method of *in vivo* lipofection.

At the end of the interview Holt talks about her work on the effects of perturbation of cell adhesion molecules on axon growth; establishing a lab; spending a year with John Gurdon at the Wellcome Cancer Research Campaign Institute in Cambridge, England; the journal review process; and balancing her career and family life and issues that women in the sciences face. The interview concludes with more of Holt's thoughts on science including the discovery that fibroblast growth factor (FGF) can prevent axons from recognizing their target; growth factor receptors' role in target recognition; and the connection of glycosaminoglycans to FGF

receptor function.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Steven J. Novak, Senior Editor, UCLA Oral History Program. B.A., History, University of Colorado; Ph.D., History, University of California, Berkeley; M.B.A., UCLA Graduate School of Management.

TIME AND SETTING OF INTERVIEW:

Place: Holt's office, University of California, San Diego.

Dates, length of sessions: October 25, 1995 (122 minutes); October 26, 1995 (112); October 27, 1995 (81).

Total number of recorded hours: 5.25

Persons present during interview: Holt and Novak.

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 consultants developed a topic outline. In preparing for this interview, Novak held a preinterview telephone conversation with Holt to obtain written background information (curriculum vitae, copies of published articles, etc.) and to agree on an interviewing schedule. He also reviewed prior Pew scholars' interviews and the documentation in Holt's file at the Pew Scholars Program office in San Francisco, including her proposal application, letters of recommendation, and reviews by Pew Scholars Program national advisory committee members. For technical background, Novak 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, 1994.

The interview is organized chronologically, beginning with Holt's childhood in Northumberland and continuing through her education in England and her career at University of California, San Diego. Major topics discussed include axon development in the retina, developing the method of in vivo lipofection, the establishment of Holt's lab, and problems faced by women in scientific careers.

ORIGINAL EDITING:

Mimi Luc, 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.

Holt reviewed the transcript. She verified proper names and made minor corrections and additions.

Kristian London, assistant editor, prepared the table of contents. Gregory M. Beyrer, editorial assistant, assembled the biographical summary and interview history. Rebecca Stone, oral history assistant, compiled the index.

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