

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

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INTERVIEWEE

*Christine E. Holt*  
(Signature)

Christine E. Holt  
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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

1982 University of California, San Diego, San Diego, California  
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

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

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

1993-1994 Wellcome Cancer Research Campaign Institute, Cambridge, England  
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.
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- Holt, C.E. et al., 1990. Lipofection of cDNAs in the embryonic vertebrate CNS. *Neuron*, 4:203-14.
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- 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 mechanospacial 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-Planck-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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