

CHEMICAL HERITAGE FOUNDATION

JEFFREY T. HOLT

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Neil D. Hathaway

at

Vanderbilt University School of Medicine
Nashville, Tennessee

on

3, 4, and 5 January 1993

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

ACKNOWLEDGEMENT

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REFORMATTING:

David J. Caruso, Program Manager, Oral History, Chemical Heritage Foundation. B.A., History of Science, Medicine, and Technology, Johns Hopkins University; Ph.D., Science and Technology Studies, Cornell University.

UNIVERSITY OF CALIFORNIA, LOS ANGELES

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Jeffrey T. Holt, M.D.
Dept. of Cell Biology
Vanderbilt University School of Medicine
Nashville, TN 37232

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

INTERVIEWEE

THE REGENTS OF THE UNIVERSITY
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(Signature)

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JEFFREY T. HOLT

1954 Born in Battle Creek, Michigan, on 24 May

Education

1976 B.A., Health Sciences, Kalamazoo College
1979 M.D., University of Michigan School of Medicine

Professional Experience

1979-1982 University of Rochester, Strong Memorial Hospital
Resident, Pathology
1982-1983 Chief Resident, Clinical Pathology

1983-1986 National Heart, Lung, and Blood Institute, National Institutes of Health
Staff Fellow, Clinical Hematology Branch
1986-1987 Senior Staff Fellow, Clinical Hematology Branch

1987-1991 Vanderbilt University School of Medicine
Assistant professor, Department of Cell Biology and Department
of Pathology
1991-present Associate professor, Department of Cell Biology and Department
of Pathology

Honors

1975 Phi Beta Kappa
1978 Alpha Omega Alpha, University of Michigan School of Medicine
1988-1992 Scholar, Pew Scholars Program in the Biomedical Sciences
1992-1994 Fogarty Fellowship
1992-present National Cancer Institute Principal Investigator
1992-present Vanderbilt Toxicology National Cancer Institute Cancer Grant

Selected Publications

Holt, J.T. et al., 1982. Elevation of the electronically determined MCV and hematocrit caused by hyperglycemia. *Journal of Clinical Pathology*, 77:56167.
Holt, J.T. et al., 1982. Inhibition of Chromium-51 red blood cell labeling by stannous

- pyrophosphate. *Journal of Nuclear Medicine*, 23:934-35.
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ABSTRACT

Jeffrey T. Holt was born and raised in Battle Creek, Michigan—the “Cereal City”—the middle child of three siblings. His father was an electrical engineer who worked for the Kellogg Company in packaging-type machines; his mother was a homemaker. Holt had what he considered a typical childhood, though he developed a great interest in playing piano and then the organ. He won a scholarship to attend the Interlochen Center for the Arts summer camp and was a finalist in the concerto competition; he also decided to play the organ for his church. Norman Rubell, a high school biology teacher who taught using the Socratic method, proved to be quite influential.

He attended Kalamazoo College in Michigan, in part because it was close to his home, intending to pursue both music and premed majors, though he ultimately gave up music. Kalamazoo did not provide any opportunities for laboratory research. Following (somewhat) in his brother’s footsteps, Holt went on to matriculate at the University of Michigan to pursue his medical doctorate. After completing medical school he went on to his residency in pathology at the Strong Memorial Hospital at the University of Rochester, before beginning postdoctoral work in the Arthur W. Nienhuis lab at the National Heart, Lung, and Blood Institute in Bethesda, Maryland, studying globin mRNA in thalassemia and investigating the effects of antisense *fos*. Some of the research in the Nienhuis lab was stymied due to leakage from the *Xenopus* oocyte nuclei which undermined transport experiments. From there he went on to a faculty position in the Departments of Cell Biology and of Pathology at the Vanderbilt University School of Medicine.

Throughout the interview Holt talks about the ways in which the practice of medicine differs from research, applying insights in pathology to cancer research, and the difficulties in applying molecular biology cancer research in practice. He also discusses how the antisense field gained acceptance and his application for a patent on a topical antisense delivery system. The interview concludes with his thoughts on applying *fos* antisense research to human cancer; searching for transcriptional differences between *c-fos* and *v-fos*; Marilyn D. Resh’s study of reticulocyte lysates and myrisylation; and Inder M. Verma’s mapping of the *fos* phosphorylation site. Holt ends the interview with reflections on his decision not to patent his HL60 leukemia cell antisense; marketing basic science research to the public; and the need to try risky experiments.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Neil D. Hathaway, Interviewer, UCLA Oral History Program. B.A., English and History, Georgetown University; M.A. and C.Phil., History, UCLA.

TIME AND SETTING OF INTERVIEW:

Place: Holt's office, Vanderbilt University School of Medicine.

Dates, length of sessions: January 3, 1993 (59 minutes); January 4, 1993 (119); January 5, 1993 (153).

Total number of recorded hours: 5.5

Persons present during interview: Holt and Hathaway.

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, from 1988 through 1992.

In preparing for this interview, Hathaway, in consultation with the director of the UCLA Oral History Program and three UCLA faculty project consultants, developed a topic outline to provide an overall interview framework. Hathaway then held a telephone preinterview conversation with Holt to obtain extensive written background information (curriculum vitae, copies of published articles, etc.) and agree on a research and interviewing timetable. Hathaway further reviewed the documentation in Holt'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, Hathaway consulted such works as: J.D. Watson et al., *The Molecular Biology of the Gene*. 4th ed. 2 vols. Menlo Park, CA: Benjamin/Cummings, 1987; Lubert Stryer, *Biochemistry*. 3d ed. New York: W.H. Freeman, 1988; *The Journal of the History of Biology*; H.F. Judson, *The Eighth Day of Creation: Makers of the Revolution in Biology*. New York: Simon and Schuster, 1979; and current issues of *Science*, *Nature*, and *Cell*.

The interview is organized chronologically, beginning with Holt's childhood and education in Battle Creek Michigan, and continuing on to his medical education at the University of Michigan School of Medicine, residency at the University of Rochester, fellowship at the National Heart, Lung, and Blood Institute, and subsequent career at the Vanderbilt University School of Medicine. Major topics discussed include Holt's specialization in pathology, his training as a physician-scientist, the comparative study of oncogenes in mice and humans, research on antisense *fos* gene, his application for a patent for a topical antisense delivery

system, and strategies for cancer research.

ORIGINAL EDITING:

Steven J. Novak, senior editor, 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.

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

Novak also prepared the table of contents, biographical summary, interview history, and index.

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