CHEMICAL HERITAGE FOUNDATION

SETH A. DARST

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Helene L. Cohen

at

The Rockefeller University
New York City, New York

on

30 April and 1, 3 May 2001

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

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.

This oral history was completed under the auspices of the Oral History Project, University of California, Los Angeles (Copyright © 2002 The Regents of the University of California) and is made possible through the generosity of

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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:

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, Biomedical Sciences and Technologies, 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. _____

This Interview Agreement is made and entered into this _____ day of _____, 2001 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 SETH A. DARST, having an address at Laboratory of Molecular Biophysics, Rockefeller University, Box 224, 1230 York Avenue, New York, New York 10021-6399, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about April 30, 2001, and tentatively entitled "Interview with Seth A. Darst." 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, including electronic reproduction, 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.

All notices and other official correspondence concerning this Agreement will be sent to the following:

If to University:

Department of Special Collections
University of California, Los Angeles
Box 951575
Los Angeles, California 90095-1575

Attention: Victoria Steele, Ph.D.

If to Interviewee:

Seth A. Darst
Laboratory of Molecular Biophysics
Box 224
1230 York Avenue
New York, New York 10021-6399

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

INTERVIEWEE

(Signature)

Seth A. Darst
(Typed Name)

Laboratory of Molecular Biophysics

1230 York Avenue

New York, NY 10021-6399

Date 5/2/01

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

(Signature)

Victoria Steele
(Typed Name)

Head, Department of Special Collections

Date 6/25/01

Pew Scholars in the Biomedical Sciences

Chemical Heritage Foundation Internet Posting Release Form

I, Seth A. Darst, 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:

a. ✓ **No restrictions for Internet Posting.**
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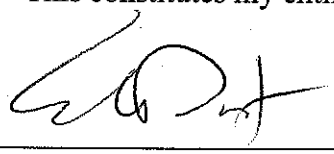

Seth A. Darst, Ph.D.

2/6/08

Date

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

SETH A. DARST

1960 Born in Alexandria, Virginia on 22 March

Education

1982 B.S., University of Colorado
1984 M.S., Stanford University
1987 Ph.D., Stanford University

Professional Experience

Stanford University
1987-1992 Postdoctoral Fellow, Department of Cell Biology

The Rockefeller University
1992-1997 Assistant Professor, Head of Laboratory
1997-2000 Associate Professor, Head of Laboratory
2000-present Professor, Head of Laboratory

Honors

1990-1996 Lucille P. Markey Award in Biomedical Science
1994-1999 Career Scientist of the Irma T. Hirschl Charitable Trust
1995-1999 Pew Scholar in the Biomedical Sciences

Selected Publications

Darst, S.A. et al., 1986. Myoglobin adsorption onto crosslinked polydimethylsiloxane. *Journal of Colloid Interface Science* 111:466-74.

Darst, S.A. et al., 1989. Three-dimensional structure of *Escherichia coli* RNA polymerase holenzyme determined by electron crystallography. *Nature* 340:730-32.

Darst, S.A. et al., 1991. Three-dimensional structure of yeast RNA polymerase II at 16 A resolution. *Cell* 66:121-28.

Stebbins, C.E. et al., 1995. Crystal structure of the GreA transcript cleavage Factor from *Escherichia coli. Nature* 373:636-40.

Polyakov, A. et al., 1995. Three-dimensional structure of *Escherichia coli* core RNA polymerase: Promoter recognition and elongation of conformations of the enzyme. *Cell* 83:365-73.

Malhotra, A., et al., 1996. Crystal structure of an *Escherichia coli* RNA polymerase σ70 subunit fragment. *Cell* 87:127-36.
Severinov, K. and S.A. Darst, 1997. A mutant RNA polymerase that forms unusual open promoter complexes. *Proceeding of the National Academy of Science USA* 94:13481-86.
Zhang, G. and S.A. Darst, 1998. Structure of the *Escherichia coli* RNA polymerase α-subunit N-terminal domain. *Science* 281:262-66.
Korzheva, N. et al., 2000. A structural model of transcription elongation. *Science* 289:619-25.
Campbell, E.A. et al., 2001. Structural mechanism for rifampicin inhibition of bacterial RNA polymerase. *Cell* (in press).

ABSTRACT

Seth A. Darst was born in Virginia, where his father was in the Army, but grew up in the Seattle, Washington area, where his father built houses and his mother taught piano. When President Carter's economic policies caused massive inflation and unemployment, Boeing Company let go many workers, and house-building was no longer a profitable business. Darst's father moved the family to Loveland, Colorado, and started another business. Seth and his brother, just a year younger, were "typical" suburban kids, riding bikes, playing baseball, goofing around, sometimes fighting with each other.

Seth's mother taught him to play the piano at an early age, and he became very good. He finished all the classes in his high school early and spent his senior year working for his father. He could not decide at first between music school and engineering school, but the difficulties inherent in a musical career persuaded him to go into chemical engineering at the University of Colorado at Boulder. He had never had to study hard before, but he learned fast in college. By the end of college he had decided that although he did not like the engineering part of chemical engineering, he did not want to go to medical school, so at the last minute he made a few telephone calls and almost accidentally ended up at Stanford University.

A required undergraduate class in biochemistry, taught by Larry Gold and Michael Yarus, had introduced him to the exciting topic of structural biology. At Stanford he worked in Roger Kornberg's lab, continuing his interest in structural biology. Near the end of his master's degree he found electron microscopy and crystallography, his ongoing interests. He was given a Lucille P. Markey Postdoctoral Fellowship, so he was able to remain in Kornberg's lab for an extra two years, just doing what he loved, until he was offered an assistant professorship at Rockefeller University.

Darst's wife, Elizabeth Campbell, was accepted into the graduate program in microbiology at Rockefeller, so the couple and their new daughter moved to New York. Elizabeth finished her PhD and now works in Seth's lab. Seth has progressed through associate professorship to full, tenured professorship, Head of Laboratory. He continues his work in prokaryotic transcription, occasionally traveling to Brookhaven or Argonne National Laboratory. He and Elizabeth balance their work with their family life as well as they can.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Helene L. Cohen, Interviewer, UCLA Oral History Program. B.S., Nursing, UCLA; P.N.P., University of California, San Diego/UCLA; M.A., Theater, San Diego State University.

TIME AND SETTING OF INTERVIEW:

Place: Darst's office, The Rockefeller University, New York.

Dates, length of sessions: April 30, 2001 (93 minutes); May 1, 2001 (99); May 3, 2001 (74).

Total number of recorded hours: 4.4

Persons present during interview: Darst and Cohen.

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, Cohen held a telephone preinterview conversation with Darst 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 Darst'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, Cohen consulted J.D. Watson et al., *Molecular Biology of the Gene.* 4th ed. Menlo Park, California: Benjamin/Cummings, 1987; Bruce Alberts et al., *Molecular Biology of the Cell.* 3rd ed. New York: Garland, 1994; Horace F. Judson, *The Eighth Day of Creation.* New York: Simon and Schuster, 1979; and recent issues of *Science* and *Nature.*

The interview is organized chronologically, beginning with Darst's childhood in Alexandria, Virginia, and continuing through his undergraduate work at University of Colorado, his graduate and postdoctoral work at Stanford University, and the establishment of his own lab at the Rockefeller University. Major topics discussed include his research in the Roger D. Kornberg lab at Stanford, his current research on prokaryotic transcription, and his lab management style.

ORIGINAL EDITING:

Deborah Kolosova, 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.

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

William Van Benschoten, senior writer, prepared the table of contents. Deborah Kolosova assembled the biographical summary and interview history. Romi Keerbs, editorial assistant, compiled the index.

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