CHEMICAL HERITAGE FOUNDATION

THOMAS C. ALBER

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Neil D. Hathaway

at

The University of California, Berkeley
Berkeley, California

on

15 March, 9 April, 16, 23, 28, and 29 July, and 15 December 1993

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 © 1997 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:

Hilary Domush, Program Assistant, Biomedical Sciences and Technologies, Chemical Heritage Foundation. B.S. Chemistry, Bates College, M.S. Chemistry, University of Wisconsin, M.A. History of Science, University of Wisconsin.

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. 970321

This Interview Agreement is made and entered into this 26th day of May, 1998 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 THOMAS C. ALBER having an address at University of California, Berkeley, Department of Molecular and Cell Biology, 229 Stanley Hall, Berkeley, California 94720, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about March 15, 1993, and tentatively entitled "Interview with Thomas C. Alber". 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. University agrees that the Work will be sealed and will not be available for public access until November 1, 2001. Notwithstanding the above, Interviewee will have the sole authority to grant access to and/or use of the Work during the period and must provide University with prior written approval of any requests therefor.

3. After November 1, 2001, University will have the right to use the Work for any research, educational or other purpose that University may deem appropriate.

4. Interviewee acknowledges that he will receive no remuneration or compensation for his 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: Thomas C. Alber
University of California, Berkeley
Department of Molecular and Cell Biology
229 Stanley Hall
Berkeley, California 94720

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

INTERVIEWEE

(Signature)

Thomas C. Alber
(Typed Name)

University of California, Berkeley
(Address)

Berkeley, California 94720

Date 3/17/96

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

(Signature)

Carli V. Rogers
(Typed Name)

Copyright Officer
(Title)

Date 5/26/98

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

THOMAS C. ALBER

1954 Born in Tokyo, Japan on 5 January

Education

1976 B.A., University of California, Santa Cruz
1981 Ph.D., Massachusetts Institute of Technology

Professional Experience

Massachusetts Institute of Technology
1981 Research Associate

University of Oregon
1982-1987 Research Associate

University of Utah
1987-1992 Assistant Professor, Associate Professor

University of California, Berkeley
1992-present Associate Professor

Honors

1975 University of California President's Undergraduate Fellowship
1976 Graduate Fellowship, Danforth Foundation
1983 Postdoctoral Fellowship, Helen Hay Whitney Foundation
1985 Fellowship, Medical Research Foundation of Oregon
1988-1992 Pew Scholar in the Biomedical Sciences

Selected Publications

Alber, T. et al., 1976. Crystal structure of elastase-substrate complex at -55 °C. *Nature* 263: 297-300.

Alber, T. et al., 1981. Crystallization of yeast triosephosphate isomerase from polyethylene glycol: Protein crystal formation following phase separation. *Journal of Biological Chemistry* 256:1356-61.

Alber, T. et al., 1981. Preliminary x-ray data for the galactose binding protein from *Salmonella*

typhimurium. Journal of Molecular Biology 147:471-74.
Alber, T. et al., 1981. On the three-dimensional structure and catalytic mechanism of triose phosphate isomerase. *Philosophical Transactions of the Royal Society of London,* Series B, Biological Sciences, 293:159-71.
Alber, T. and G. Kawasaki, 1982. Nucleotide sequence of the triose phosphate isomerase gene of *Saccharomyces cerevisiae. Journal of Molecular and Applied Genetics* 1:419-34.
Alber, T. et al., 1983. The role of mobility in the substrate binding and catalytic machinery of enzymes. *CIBA Foundation Symposia* 93:4-24.
Alber, T. and J.A. Wozniak, 1985. A genetic screen for mutations that increase the thermal stability of phage T4 lysozyme. *Proceedings of the National Academy of Sciences USA* 82:747-50.
Alber T. et. al., 1986. Structure and stability of mutant lysozymes from bacteriophage T4. In *Protein Structure, Folding, and Design,* UCLA Symposia on Molecular and Cellular Biology, vol 39. New York: Alan R. Liss, 307-18.
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Alber, T. and B.W. Matthews, 1987. The use of x-ray crystallography to determine the relationship between the structure and stability of mutants of phage T4 lysozyme. In *Protein Engineering,* eds. D.L. Oxender and C.F. Fox. New York: Alan R. Liss, 289-98.
Alber, T. et al., 1987. Temperature-sensitive mutations of bacteriophage T4 lysozyme occur at sites with low mobility and low solvent accessibility in the folded protein. *Biochemistry* 26:3754-58.
Alber, T. et al., 1987. Contributions of hydrogen bonds of Thr157 to the thermodynamic stability of phage T4 lysozyme. *Nature* 330:41-46.
Alber, T. et al., 1987. Crystallography and site-directed mutagenesis of yeast triose phosphate isomerase: What can we learn about catalysis from a "simple" enzyme. *Cold Spring Harbor Symposia on Quantitative Biology* 52:603-13.
Alber, T. and B.W. Matthews, 1987. Structure and thermal stability of phage T4 lysozyme. *Methods in Enzymology* 154:511-33.
Alber, T. et al., 1988. Replacements of pro^{86} in phage T4 lysozyme extend an α helix but do not alter protein stability. *Science* 239:631-35.
Alber, T., 1989. Mutational effects on protein stability. *Annual Review of Biochemistry* 58:765-98.
Alber, T., 1992. Structure of the leucine zipper. *Current Opinion in Genetics and Development* 2:205-10.
Alber, T., 1993. How GCN4 binds DNA. *Current Biology* 3:182-84.

ABSTRACT

Thomas C. Alber grew up as an American in post World War II Japan and had to deal with issues related to his bilingualism and biculturalism. After moving to Los Angeles with his mother in 1964, Alber was encouraged in all areas of study, including the sciences, through his involvement with the Independent Program School at University High School in Los Angeles. This unique high school experience helped Alber choose the University of California, Santa Cruz for his undergraduate studies because of its non-traditional structure. At Santa Cruz, Alber worked in Anthony L. Fink's enzyme mechanism laboratory and pursued an opportunity to perform research with Gregory A. Petsko at Wayne State University. This research experience solidified his future interests in chemistry and biochemistry over other fields, such as the history of science. With a Danforth Foundation Graduate Fellowship, Alber undertook graduate research at the Massachusetts Institute of Technology (MIT), first under Alexander Rich and later under Petsko (when Petsko joined the MIT faculty). Alber traveled as a graduate student to do research at various laboratories including those at the University of California, San Diego, the University of California, Berkeley, and the University of Oxford. After earning his Ph.D., Alber started his postdoctoral research with Brian W. Matthews at the University of Oregon. Since Matthews was involved with the interdisciplinary Institute of Molecular Biology, Alber continued his pattern of research and study in a non-traditional setting. While finishing his postdoctoral research, Alber authored "Mutational effects on Protein Stability," in the *Annual Review of Biochemistry* in 1989. In this article, he proposed departing from the traditional model system of structural protein research and instead stressed the importance of all possible hydrogen-binding sites, the external amino acids on the rigid portion of the active site, the relative unimportance of the so-called 'floppy part,' and the necessity for flexibility in a protein. Alber's movement from the University of Oregon to the University of Utah and then on to the University of California, Berkeley allowed him to reflect on the American model of university science, the ways in which that model differs at a range of institutions, and the ways in which it varies from science in other nations. Alber's oral history ends with a discussion of the ways in which Alber's laboratory life changed over a ten-month period in 1993 right after he joined the faculty at Berkeley.

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: Alber's office, University of California, Berkeley.

Dates, lengths of sessions: March 15, 1993 (75 minutes); April 9, 1993 (85) ; July 16, 1993 (93) ; July 23, 1993 (83) ; July 28, 1993 (85) ; July 29, 1993 (108) ; December 15, 1993 (76).

Total number of recorded hours: 10

Persons present during interview: Alber 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' 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 and the director of the UCLA Oral History Program then held an in-person pre interview conversation with Alber 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 Alber'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;* and H.F. Judson, *The Eighth Day of Creation: Makers of the Revolution in Biology.* New York: Simon and Schuster, 1979.

The interview is organized chronologically, beginning with Alber's childhood and education in Tokyo and Los Angeles and continuing through his education, his postdoctoral work at the University of Oregon, and his career at the University of Utah and University of California, Berkeley. Major topics discussed include low-temperature x-ray crystallography, protein structure and folding, and the training and funding of research scientists.

ORIGINAL EDITING:

Kristian T. London, 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.

Alber declined to review the transcript but did respond to editorial queries by telephone.

Steven J. Novak, senior editor, prepared the table of contents and index. London assembled the biographical summary and interview history.

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