CHEMICAL HERITAGE FOUNDATION

RONALD A. MILLIGAN

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Neil D. Hathaway

at

Scripps Research Institute
La Jolla, California

on

22 and 24 October and 17 December 1992

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. R921105

This Interview Agreement is made and entered into this 7th day of November, 1992 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 RONALD A. MILLIGAN having an address at Scripps Clinic and Research Foundation, 10666 North Torrey Pines Road, La Jolla, California, 92037, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about October 23, 1992, and tentatively entitled "Interview with Ronald A. Milligan". 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 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.

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

If to University : Office of Intellectual Property Administration
University of California, Los Angeles
405 Hilgard Avenue
Los Angeles, California 90024-1406

Attention: Ms. Carli V. Rogers
Copyright Officer

If to Interviewee: Ronald A. Milliagan
Scripps Clinic & Research Foundation
10666 No. Torrey Pines Road
La Jolla, CA 92037

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

INTERVIEWEE

(Signature)

Ronald A. Milligan
(Typed Name)

Scripps Clinic and Research Foundation

10666 N. Torrey Pines Road
(Address)

La Jolla, CA 92037

Date 23 OCT 92

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

(Signature)

Carli V. Rogers
(Typed Name)

Copyright Officer

(Title)

Date November 7, 1992

Chemical Heritage Foundation
Oral History Program
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RONALD A. MILLIGAN

1954 Born in Londonderry, Northern Ireland, on 9 May

Education

1975 B.Sc., Plant Science and Microbiology, Leeds University
1984 Ph.D., Cell Biology, Stanford University

Professional Experience

Nuffield Institute of Comparative Medicine, London, England
1975-1978 Research Assistant

Medical Research Council (MRC) Laboratory of Molecular Biology, Cambridge, England
1978-1980 Research Assistant

Stanford University
1984-1987 Postdoctoral Fellow

European Molecular Biology Laboratory (EMBO), Heidelberg, Germany
1985 Postdoctoral Fellow

Scripps Research Institute, La Jolla, California
1987-1993 Assistant Member
1993-present Associate Member

Honors

1981-1984 SERC/NATO Overseas Studentship
1982-1983 EMBO Short Term Fellowship
1985 Royal Society Postdoctoral Fellowship
1987 EMSA Burton Medal
1988-1992 Pew Scholars Program in the Biomedical Sciences
1989 National Institutes of Health DRR and NHLBI Special Study Sections
1991-present Editorial Board, *Journal of Structural Biology*
1991-1992 Peer Review Committee, American Heart Association, California Affiliate

1992-1993	National Institutes of Health DRR and NHLBI Special Study Sections
1992-1997	Established Investigator, American Heart Association

Selected Publications

Unwin, P.N.T. and R.A. Milligan, 1982. A large particle associated with the perimeter of the nuclear pore complex. *Journal of Cell Biology,* 93:63-75.

Milligan, R.A. and P.N.T. Unwin, 1982. *In vitro* crystallization of ribosomes from chick embryos. *Journal of Cell Biology,* 95:648-53.

Milligan, R.A. and A. Brisson, P.N.T. Unwin, 1984. Molecular structure determination of crystalline specimens in frozen aqueous solutions. *Ultramicroscopy,* 13:1-10.

Taylor, K.A., R.A. Milligan, C. Raeburn and P.N.T. Unwin, 1984. A cold stage for the Philips EM300. *Ultramicroscopy,* 13:185-90.

Milligan, R.A. and P.N.T. Unwin, 1986. Location of exit channel for nascent protein in 80S ribosome. *Nature,* 319:693-95.

Milligan, R.A., 1986. A structural model for the nuclear pore complex. In *Nucleo-cytoplasmic Transport,* eds. R. Peters and M. Trendelenberg. Heidelberg: Springer-Verlag, p. 113-22.

Milligan, R.A. and P.F. Flicker, 1987. Structural relationships of actin, myosin and tropomyosin revealed by cryo-electron microscopy. *Journal of CellBiology,* 105:29-39.

Milligan, R.A., M. Whittaker and D. Safer, 1990. Molecular structure of F-actin and location of surface binding sites. *Nature,* 348:217-21.

Mandelkow, E.M., E. Mandelkow and R.A. Milligan, 1991. Microtubule dynamics and microtubule caps: A time-resolved cryo-electron microscopy study. *Journal of Cell Biology,* 114:977-91.

Flicker, P.F., R.A. Milligan and D. Applegate, 1991. Cryoelectron microscopy of S1-decorated actin filaments. *Advances in Biophysics,* 27:185-95.

Hessler, E., S.J. Young, B.O. Carragher, M. Martone, J.E. Hinshaw, R.A. Milligan, E. Masliah, M. Whittaker, S. Lamont and M.H. Ellisman, 1992. SYNU: Software for visualization of 3-dimensional biological structures. In *Microscopy: The Key Research Tool,* eds. C.E. Lyman, L.D. Peachey and R.M. Fisher, published by EMSA Inc. 22:73-82.

Hinshaw, J.E., B.O. Carragher and R.A. Milligan, 1992. Architecture and design of the nuclear pore complex. *Cell,* 69:1133-41.

Holmes, K.C., M. Tirion, D. Popp, M. Lorenz, W. Kabsch and R.A. Milligan, 1992. A comparison of the atomic model of F-actin with cryo-electron micrographs of actin and decorated actin. In *Mechanism of Myofilament Sliding in Muscle Contraction,* eds. H. Sugi and G.H. Pollack. Plenum Publishing Corp (in press).

Ray, S., E. Meyhöfer, R.A. Milligan and J. Howard, 1993. Kinesin follows the microtubule's protofilament-axis. *Journal of Cell Biology,* (in press).

ABSTRACT

Ronald A. Milligan grew up on a farm outside of Londonderry, Northern Ireland, the youngest of five children. Life was, in his words, "primitive." He spent most of his free time outside, never feeling bored. He was interested in birdwatching, eventually in hunting birds. He passed his 11+ exam, attended grammar school, and went on to university, the first in his family.

He had been interested in biology all through his childhood, and when a school trip to Queen's University in Belfast exposed him to bacteriology, he decided he wanted to study botany and bacteriology. His scores admitted him to the University of Leeds. He had made the decision to be a research scientist earlier, though he does not remember how he learned what a scientist did. During his teenage years religious conflict in Northern Ireland became extreme; there was the outbreak of terrorism and British military occupation. Milligan was graduated with a lower second-class honors degree and began to hunt for a job. He took a position as a research assistant at the Nuffield Institute of Comparative Medicine at the London Zoo, where he studied botulism and bovine pleuropneumonia. From there he became a research assistant at the Medical Research Council (MRC Laboratory of Molecular Biology in Cambridge, England, going to work on nuclear pore complex (NPC) in Nigel Unwin's lab. When Unwin was recruited to Stanford, Milligan went along as a graduate student. Here Milligan discusses Unwin's reasons for leaving MRC and his [Unwin's] own experiences at Stanford. Milligan goes into detail about his work on low-temperature ribosome crystallization and how electron microscopes damage specimens. He spent three months in Heidelberg, Germany, studying cryo-electron microscopy; his results allowed him to acquire independence as a researcher. Milligan talks about his NPC research, grantsmanship, and "safe science"; he explains his work of freezing specimens in amorphous ice and the damage caused by electron microscopy and by freezing; he goes into methods of enhancing imaging, synthetic universe visualization software, omega energy filtering microscopes, field emission guns, atomic force microscopy, and relations with competitors; and he continues with explanations of cell symmetry and the structure of the NPC and NPC intermediate structures.

Milligan's research continued with studying muscle cell structure with cryo-electron microscopy, and he collaborated with Paula F. Flicker: there was a lack of evidence for the cross-bridge muscle cycle theory but a discovery of new myosins. He attended cell biology conferences and spent money setting up a lab. He conceived an interest in molecular motors and talks about microtubule dynamics.

Milligan winds down his interview with answers to general questions: he talks about the need to work in the mainstream of scientific research; personnel in his lab; the role of computers; how funding trends shape research; the autonomy provided by Scripps Research Institute; Milligan's raison d'être; pure science and applied science; scientists' motivations; Scripps's ties to Johnson and Johnson; how Scripps recruited Milligan; and the Scripps administration. He finishes with insight into his marriage and thoughts about his future.

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: Milligan's office, Scripps Research Institute, La Jolla, California.

Dates, length of sessions: October 22, 1992 (126 minutes); October 24, 1992 (127); December 17, 1992 (200).

Total number of recorded hours: 7.55

Persons present during interview: Milligan 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 five-year Pew scholarships, from 1988 through 1992.

In preparing for this interview, Hathaway, in consultation with the directory 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; in-person] preinterview conversation with Milligan 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 Milligan's file at the Pew Scholars offices in San Francisco, including his proposal application, letters of recommendation, and evaluations by Pew Scholars program board members. Hathaway also acquired general knowledge of contemporary work on oncogenesis and on the cell biological and biochemical approaches used to elucidate protein transport in *Saccharomyces cervisiae*, and relied on the following works for background on the recent history of the biological sciences: J.D. Watson, N.H. Hopkins, et al., *The Molecular Biology of the Gene*, [2 volumes in 1] , (Menlo Park, CA, 1987); Lubert Stryer's *Biochemistry* (New York, 1988), historical sources, e.g., *The Journal of the History of Biology* and H.F. Judson's *The Eighth Day of Creation* (New York, 1979).

The interview is organized chronologically, beginning with Milligan's childhood and education in Northern Ireland, continuing through his work at the Nuffield Institute of Comparative Medicine in London, the Medical Research Council Laboratory in Cambridge, England, his graduate education at Stanford University, and his subsequent career at Scripps Research Institute in La Jolla, California. Major topics discussed include electron microscopes,

nuclear pore complexes, ribosome crystallization, myosins and microtubules, and Milligan's reflections on scientific research.

ORIGINAL EDITING:

Steven J. Novak, 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.

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

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

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