# 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

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

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# **REFORMATTING:**

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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."

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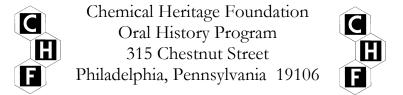
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# **RONALD A. MILLIGAN**

1954	Born in Londonderry, Northern Ireland, on 9 May					
Education						
1975 1984	B.Sc., Plant Science and Microbiology, Leeds University Ph.D., Cell Biology, Stanford University					
Professional Experience						
1975-1978	Nuffield Institute of Comparative Medicine, London, England Research Assistant					
1978-1980	Medical Research Council (MRC) Laboratory of Molecular Biology, Cambridge, England Research Assistant					
1984-1987	Stanford University Postdoctoral Fellow					
1985	European Molecular Biology Laboratory (EMBO), Heidelberg, Germany Postdoctoral Fellow					
1987-1993 1993-present	Scripps Research Institute, La Jolla, California Assistant Member Associate Member					
<u>Honors</u>						
1981-1984 1982-1983 1985 1987 1988-1992 1989 1991-present 1991-1992	SERC/NATO Overseas Studentship EMBO Short Term Fellowship Royal Society Postdoctoral Fellowship EMSA Burton Medal Pew Scholars Program in the Biomedical Sciences National Institutes of Health DRR and NHLBI Special Study Sections Editorial Board, <i>Journal of Structural Biology</i> Peer Review Committee, American Heart Association, California Affiliate					

# **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.
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- 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.
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- 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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