

CHEMICAL HERITAGE FOUNDATION

PAUL J. ANDERSON

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Steven J. Novak

at

Dana-Farber Cancer Institute
Boston, MA

on

18, 19, and 22 May 1995

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

ACKNOWLEDGEMENT

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Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about May 18, 1995, and tentatively entitled "Interview with Paul J. Anderson". 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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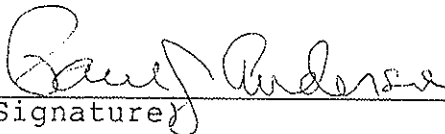
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Brigham & Women's Hospital
Department of Rheumatology & Immunology
75 Francis Street
Boston, MA 02115

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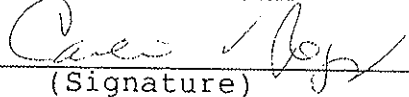
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PAUL J. ANDERSON

1956 Born in Syracuse, New York on 25 November

Education

1978 B.S, Biology, State University of New York at Stony Brook
1983 Ph.D., Biochemistry, New York University
1984 M.D., New York University

Professional Experience

Brigham and Women's Hospital, Boston
1984-1985 Intern
1985-1986 Resident

Brigham and Women's Hospital and Dana-Farber Cancer Institute
1986-1990 Clinical and Research Fellow

Harvard University Medical School, Boston
1988-1990 Instructor
1990-1994 Assistant Professor
1994-present Associate Professor

Honors

1978 Phi Beta Kappa
1978 Medical Scientist Training Program Fellowship
1980 Woods Hole Marine Biological Laboratory Prize
1981 New York Arthritis Foundation Summer Fellowship
1984 Alpha Omega Alpha
1987 Loeb Award, Arthritis Foundation
1990-1994 Pew Scholar in the Biomedical Sciences
1990 Cancer Research Institute Investigator Award
1994 Distinguished Alumnus Award, State University of New York at
Stony Brook
1995 Leukemia Scholar Award

Selected Publications

- Anderson, P. and W. Bauer, 1978. Supercoiling in closed circular DNA: Dependence upon ion type and concentration. *Biochemistry*, 17:594-601.
- Anderson, P. et al., 1981. Entrapment of human leukocyte interferon in the aqueous interstices of liposomes. *Infection and Immunity*, 31:1099-1103.
- Anderson, P. et al., 1982. Effect of primary amines on interferon action. *Virology*, 117:510-15.
- Anderson, P. et al., 1982. Specific binding of ¹²⁵I-human interferon-gamma to high affinity receptors on human fibroblasts. *Journal of Biological Chemistry*, 257:11301-4.
- Anderson, P. and J. Vilek, 1982. Synthesis and biological characterization of a covalent conjugate between interferon and ricin toxin B chain. *Virology*, 123:457-60.
- Anderson, P. et al., 1983. Human interferon-gamma is internalized and degraded by cultured fibroblasts. *Journal of Biological Chemistry*, 258:6497-502.
- Anderson, P. and C. Nagler, 1984. Photoaffinity labeling of interferon-gamma receptor on the surface of cultured fibroblasts. *Biochemical and Biophysical Research Communications*, 120:828-33.
- Anderson, P. et al., 1987. Crosslinking T3 (CD3) with T4 (CD4) enhances the proliferation of resting T lymphocytes. *Journal of Immunology*, 139:678-82.
- Anderson, P. et al., 1988. Comodulation of CD3 and CD4: Evidence for a specific association between CD4 and approximately 5% of the CD3: T cell receptor complexes on helper T lymphocytes. *Journal of Immunology*, 140:1732-37.
- Anderson, P. et al., 1988. Crosslinking CD3 with CD2 using cepharose immobilized antibodies enhances T lymphocyte proliferation. *Cellular Immunology*, 115:246-56.
- Anderson, P. et al., 1989. Monoclonal antibodies reactive with the T cell receptor ζ chain: Production and characterization using a new method. *Journal of Immunology*, 143:1899-1904.
- Anderson, P. et al., 1989. CD3-negative natural killer cells express TCR ζ as part of a novel molecular complex. *Nature*, 341:159-62.
- Anderson, P. et al., 1990. A monoclonal antibody reactive with a 15 kd cytoplasmic granule-associated protein defines a subpopulation of CD8⁺ T lymphocytes. *Journal of Immunology*, 144:574-82.
- Anderson, P. et al., 1990. Fc γ receptor type III (CD16) is included in the ζ NK receptor complex expressed by human natural killer cells. *Proceedings of the National Academy of Sciences USA*, 87:2274-78.
- Taupin, J.L. and P. Anderson, 1994. Activation-induced proteolysis of the cytoplasmic Domain of ζ in T cell receptors and Fc receptors. *European Journal of Immunology*, 24:3000-3004.

ABSTRACT

Paul J. Anderson, the oldest of four children, was born in 1954; he grew up in a suburb of Syracuse, New York. His father was a school teacher and administrator, his mother a housewife. He discovered a love of science when he was about 10 years old, a love he nurtured through his B.S. degree in biology from the State University of New York (SUNY), Stony Brook in 1978. Biochemistry professor Bernard Dudock inspired Anderson to work part time in William Bauer's labs, where he was encouraged to design his own experiments, an unusual practice for undergraduates. At that time Bauer was working on DNA, and in his labs Anderson met Francis Crick. Anderson also was able to publish some articles about his work in those labs.

He then entered a joint MD/PhD program at New York University (NYU), receiving his MD in 1983 and his PhD in 1984. Interested in immunology, he specialized in rheumatology for his two clinical years at Brigham and Women's Hospital in Boston. During this period he became involved in the excitement of working on interferon and interferon receptors. He also began working at Stuart F. Schlossman's lab at the Dana-Farber Cancer Institute, where work was being done on different subpopulations of T lymphocytes in the peripheral blood.

Schlossman became a mentor to Anderson, whose biochemical background and focus on immunology led him to develop an assay to identify intracellular antigens. This involved developing a cytometric flow assay to screen for monoclonal antibodies. Anderson observed that natural killer cells express zeta, an antibody that reacts with cytotoxic lymphocytes. He tracked the antigen causing transplant rejection to cytotoxic granules, reinforcing the theory that the antibody could recognize a toxic molecule. It became clear that the full-length RNA-binding protein is involved somehow in signaling apoptotic death in cytotoxic lymphocyte target cells, and we now know in all cells. He helped found the biotechnology company Apoptosis Technology as a subsidiary of Immunogen; he has several patents.

Anderson finds science unpredictable when he enters new areas; this is exciting to him and is one of the main reasons he continues to love research science. He believes we will continue to learn more about the molecular mechanisms of apoptosis, which will allow us to interfere in the molecular cell death and thereby to control or cure various diseases and health problems like cancer or organ rejection.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Steven J. Novak, Senior Editor, UCLA Oral History Program. B.A., History, University of Colorado; Ph.D., History, University of California, Berkeley; M.B.A., UCLA Graduate School of Management.

TIME AND SETTING OF INTERVIEW:

Place: Anderson's office, Dana-Farber Cancer Institute, Boston.

Dates, length of sessions: May 18, 1995 (112 minutes); May 19, 1995 (96); May 22, 1995 (70).

Total number of recorded hours: 4.6

Persons present during interview: Anderson and Novak.

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 consultants developed a topic outline. In preparing for this interview, Novak held a telephone pre interview conversation with Anderson to obtain extensive written background information (curriculum vitae, copies of published articles, etc.) and agree on a research and interviewing timetable. Novak further reviewed the documentation in Anderson'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, Novak consulted such works as: J.D. Watson et al., *The Molecular Biology of the Gene*. 4th ed. Menlo Park, CA: Benjamin/Cummings, 1987 and Bruce Alberts et al., *Molecular Biology of the Cell*. 3d ed. New York: Garland, 1994.

The interview is organized chronologically, beginning with Anderson's childhood in Syracuse, New York, his education, internship, and residency, and the establishment of own laboratory at Dana-Farber Cancer Institute. Major topics discussed include interferon, T cell receptors, cytotoxic lymphocytes, apoptosis, immunology, rheumatology, and the biotechnology industry.

ORIGINAL EDITING:

Vimala Jayanti, editor, 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

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

Jayanti assembled the biographical summary. The interviewer prepared the table of contents, interview history, and index.

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<p>Grew up in Syracuse, NY. Had nurturing, happy childhood; three siblings; engaged in casual childhood activities. Early interest in science. Expectations of college; entered SUNY Stony Brook; eyes opened to provinciality of childhood. Worked in William Bauer's lab, given much autonomy. Studies nicking-closing enzyme that opens supercoiled DNA.</p>	
College and Graduate School	15
<p>Discovered that caotropic salt solution alters the winding of DNA. Anderson published his first scientific paper. Felt that opportunities for scientific discovery are always present. Entered the New York University M.D/Ph.D. program. Enjoyed life in Manhattan. Met Cathryn Nagler, now his wife. Her scientific background and research. The decreasing usefulness of the combined M.D./Ph.D. degree. Spent summers in the Gerald Weissmann lab. at Woods Hole Marine Biological Laboratory. Excited by studying interferon in the Jan Vilek lab, where he worked on interferon receptors. Performed internship and residency in internal medicine at Brigham and Women's Hospital in Boston, where he specialized in rheumatology.</p>	
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<p>Entered Stuart F. Schlossman's lab at the Dana-Farber Cancer Institute. Schlossman defined different subpopulations of T lymphocytes in the peripheral blood and characterized the T cell receptor complex. Monoclonal antibody technology. Flow cytometry technology. Schlossman as mentor. Description of work pace of modern scientific research. Life in the Boston region. Teaching efforts with students and postdocs. Inevitability of scientific progress. Anderson's background in Biochemistry. His continued focus on immunology. Schlossman students who have become leaders in the field. Schlossman's management style. Schlossman convened congresses to characterize antibody reagents and provide them with cluster designations. Anderson developed an assay to identify intracellular antigens and studied the role of the zeta subunit in the immune response. Observed that natural killer cells also express zeta. Discovered an antibody that reacts with cytotoxic lymphocytes and tracked the antigen causing transplant rejection to cytotoxic granules.</p>	
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<p>Identified RNA-binding proteins. Explored the relationship between TIA-1 and apoptosis. How apoptosis differs from necrosis. Searched for genes that trigger apoptosis. Role of the Fas protein in apoptosis. How phosphorylation affects the activity of TIA-1. The unpredictable nature of</p>	

research. Collaborations with Rolf Kiessling and Michel Streuli.
Anderson's patents. Founded the biotechnology company Apoptosis
Technology as a subsidiary of Immunogen; his role in the company. Role of
the immune system in fighting cancer. Risks involved in chemotherapy and
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residues. More on Anderson's patents. More on Apoptosis Technology.
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Training of Ph.D.'s in the basic sciences. Serving on study sections.
Reviewing papers for scientific journals. The rejection and frustration
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