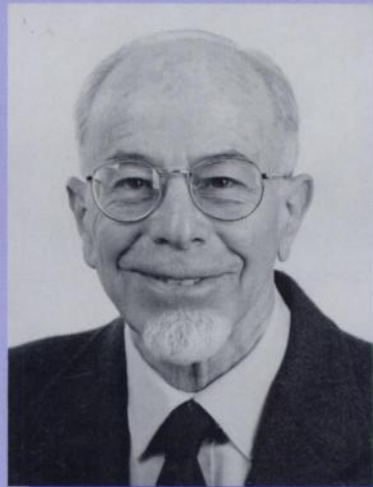
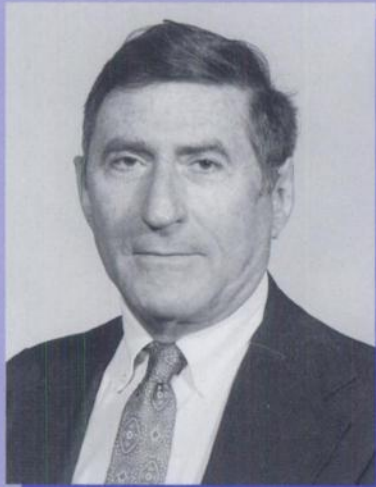




Cancer Research

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Ubiquitin is a multifunctional and extremely conserved protein (~8.5 kD). Ubiquitin has the unusual property of linking to a lysine e-amino group in another protein to produce a covalent ubiquitin conjugate. Such conjugates are usually very unstable, being recognized by a specific ubiquitin dependent protease and rapidly degraded. Ubiquitin therefore appears to target such proteins for rapid degradation. There are also examples of stable ubiquitin conjugates, i.e. Histone H2a and some unusual forms of actin. Several groups have noted that a variety of pathological inclusions found in many human disease states exist as stable ubiquitin conjugates. These inclusions include the neurofibrillary tangles of Alzheimer's disease and progressive supranuclear palsy, Pick bodies of Pick's disease, Lewy bodies of Parkinson's disease, Mallory bodies of alcoholic liver disease, Rosenthal fibers of Alexander's disease, and the inclusion bodies in inclusion myositis and oculopharyngeal muscular dystrophy.

Useful for:

- ◆ ELISA
- ◆ Immunohistochemistry
- ◆ Immunoprecipitation
- ◆ Western Blotting

References:

1. Manetto V et al; *Proc Natl Acad Sci USA* 85:4501 (1988)
2. Shaw G and Chau V; *Proc. Natl. Acad. Sci. USA* 85:2854 (1988)
3. Mayer RJ et al; *Ann NY Acad Sci* 674:149 (1992)
4. Schmidt ML et al; *Am J Pathol* 139: 53 (1991)
5. Askanas et al; *Neurosci Lett* 130:73 (1991)

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BENEFITS OF MEMBERSHIP



The American Association for Cancer Research (AACR) is a scientific society consisting of laboratory and clinical cancer researchers. It was founded in 1907 and its purposes are "to facilitate communication and dissemination of knowledge among scientists and others dedicated to the cancer problem; to foster research in cancer and related biomedical sciences; to encourage presentation and discussion of new and important observations in the field; to foster public education, science education, and training; and to advance the understanding of cancer etiology, prevention, diagnosis, and treatment throughout the world." Members of the AACR enjoy the following benefits:

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Chairman

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COVER LEGEND



After the introduction of monoclonal antibodies in the late 1970s, their use developed rapidly. Today, monoclonal antibodies are used for the typing of human leukemias and lymphomas, and they represent an invaluable tool in the diagnosis and treatment of those forms of cancer. This issue's cover features the pioneer investigators who discovered the relevant antigens in the mouse.

The first cell surface antigen used widely in the typing of mouse lymphocytes was discovered by Arnold E. Reif (*center*) and his research assistant Joan Allen, a recent graduate of a junior college [*Nature (Lond.)*, 200: 1332, 1963]. They produced antibodies specific for thymic lymphoma with unexpectedly strong reactivity against both lymphoma and normal thymus cells. This unusual antibody reacted with an antigen (later named Thy-1 by Dr. Reif) abundant on the cell surface of thymus cells, thymus-derived leukemias, and nervous tissues (*J. Exp. Med.*, 120: 413, 1964). Drs. Reif and Allen used antibodies to Thy-1 to first demonstrate that antibodies could differentiate between normal and leukemic lymphocytes (*Cancer Res.*, 26: 123, 1966).

In their 1964 paper, Drs. Reif and Allen suggested that Thy-1 is a marker not only for thymus cells but also for thymus-derived peripheral lymphocytes; this proof was vital, however, before antibodies to Thy-1 could be used to identify such cells with certainty. The first evidence that this was true was published by Michael Schlesinger (*left*) and I. Yron, who reported that rabbit anti-thymocyte serum eliminated a Thy-1-carrying subpopulation of lymph node cells [*Science (Washington DC)*, 164: 1412, 1969]. Seventeen days after this paper appeared, Martin C. Raff reported similar findings but more definitive conclusions [*Nature (Lond.)*, 224: 378, 1969]. In June 1970, papers in the same issue of *Nature* by Dr. Schlesinger (226: 1254), Dr. Raff (226: 1257), and A. Schimpl and E. Wecker (226: 1258) showed that mature murine T cells can be selectively killed *in vivo* with anti-Thy-1 serum. That Thy-1-positive cells could also be depleted by neonatal thymectomy was proved in papers submitted on the same day by Drs. Schlesinger and Yron (*J. Immunol.*, 104: 798, 1970) and by Drs. Raff and H. H. Wortis (*Immunology*, 18: 931, 1970). Thus, the

presence of Thy-1 on peripheral T cells as well as the use of Thy-1 antibodies for the selective *in vivo* depletion of these cells had been demonstrated.

Göran Möller (*right*) showed earlier that a large proportion (but not all) of mouse lymphocytes expressed membrane-bound immunoglobulin, produced by the lymphocytes and not passively absorbed (*J. Exp. Med.*, 114: 415, 1961). Raff *et al.* confirmed these results and showed that these same lymphocytes were B cells (*Immunology*, 19: 637, 1970; *Nat. New Biol.*, 223: 225, 1971). Thus, Thy-1 and membrane immunoglobulin became the first and still-used markers for T and B cells. Since these are key cells in the immune response, it was now possible to dissect it into its cellular components.

L. J. Old, E. A. Boyse, and E. Stockert reported the murine lymphocyte antigen TL a few months before Thy-1 was discovered (*J. Natl. Cancer Inst.*, 31: 977, 1963), but TL was not a marker for T cells [Reif, A. E., and Schlesinger, M. (eds.), *Cell Surface Antigen Thy-1*. New York & Basel: Marcel Dekker, 1989].

Dr. Reif is Research Professor of Pathology, Emeritus, at Boston University School of Medicine, where he was Chief of the Laboratory of Experimental Cancer Immunotherapy at the Mallory Institute of Pathology. He was trained in cancer research by Van R. Potter at the McArdle Laboratory for Cancer Research in Madison, WI (1950–1952), and in immunology by Michael Heidelberger (1956). He has published over 100 articles and book chapters, and he has edited or coedited 3 books, including *Immunity and Cancer in Man: An Introduction* (New York & Basel: Marcel Dekker, 1975). He cochaired the first Conference on Immunity to Cancer in 1984 and was President of the Boston Cancer Research Association in 1990–1991. Dr. Reif received B.A. and M.A. degrees from the University of Cambridge, England (1945 and 1949, respectively), M.S. and D.Sc. degrees from Carnegie-Mellon University in Pittsburgh, PA (1949 and 1950, respectively), and an M.T.S. degree from the Divinity School, Harvard University, Cambridge, MA, in 1993.

Dr. Schlesinger is Lady David Professor of Experimental Medicine and Cancer Research as well as Chairman of the Paul Ehrlich Center for the Study of Leukemic and Normal White Blood Cells at the Hebrew University-Hadassah Medical School in Jerusalem, Israel. From 1977 to 1982, he served as Vice President of the Hebrew University of Jerusalem. The author or coauthor of more than 180 papers and book chapters, he has chaired several conferences on immunology and transplantation and serves as President of the Israel Society of Immunology. Dr. Schlesinger received the M.D. degree (1958) from the Hebrew University-Hadassah Medical School.

Dr. Möller received the M.D. and Ph.D. degrees from the Karolinska Institute in 1963. He was Professor of Immunology at the Karolinska Institute from 1969 to 1985, and thereafter Professor of Immunology at Stockholm University. He has been a member of the Nobel Committee and the Nobel Assembly at the Karolinska Institute, and he was Vice Chairman of the Nobel Assembly in 1985. He received the Jahre Prize (Oslo, Norway) for Medical Research in 1976. He is an honorary member of the American Association for Immunology. In 1961, Dr. Möller discovered that B lymphocytes carried on their membranes immunoglobulin molecules made by lymphocytes.

We are indebted to Drs. Reif, Schlesinger, and Möller for supplying us with information and photographs for this cover feature.

Edwin A. Mirand