

The specific notion

Fred S. Rosen

Exquisite Specificity: The Monoclonal Antibody Revolution. By Alberto Cambrosio and Peter Keating. *Oxford University Press: 1996. Pp. 243. £39.50, \$59.95.*

EVER since Dr Charles McIntyre collected a urine specimen from a greengrocer with myeloma in Devonshire Street, London, in 1846, the study of the disease has been a productive route to discovery. McIntyre, thinking that the greengrocer's urine would contain protein ("animal matter") because he was losing weight rapidly, heated the urine and found that a precipitate formed between 45 °C and 60 °C, which redissolved when the urine was boiled. He then sent this urine specimen to Professor Henry Bence-Jones, at Guy's Hospital, asking "What is this?". Bence-Jones never answered, but the precipitate nevertheless became known as Bence-Jones protein. It was only the second protein to be obtained in pure form (the first having been hen egg albumin). It was more than a century later that Bence-Jones proteins were identified as the light chains of immunoglobulins.

Myelomas are tumours of plasma cells, usually in the bone marrow. They are found in many species, and can be induced in mice by intraperitoneal injection of mineral oil. Myeloma proteins, which are immunoglobulins secreted by malignant plasma cells, eventually helped to solve problems of immunoglobulin genetics and structure. Gerald Edelman shared the Nobel Prize for Physiology or Medicine in 1972 after completing the sequence of a myeloma protein, Eu, the first immuno-globulin to be sequenced completely.

In 1975, a landmark paper was published by Georges Köhler and César Milstein (*Nature* **256**, 495; 1975). These investigators fused mouse myeloma cells with splenic lymphocytes from a mouse that had been immunized with sheep red blood cells. The immortalized hybrid cells now produced prodigious quantities of pure monoclonal antibodies to sheep red blood cells. Standardized reagents, hitherto unknown in immunology, were now available. Several immunologists in the early 1970s were trying to establish monoclonal antibody production by transformed cells, but Köhler and Milstein were the first to succeed.

They grasped the power of this new tool, but could not anticipate that it would spawn a multimillion-dollar biotechnology industry, which came about largely

because of the almost simultaneous development of the fluorescence-activated cell sorter. Monoclonal antibodies worth \$574 million are said to have been sold in the United States alone in 1992. This transformation of a simple and beautiful discovery into a vast biotechnology industry is now recounted by Alberto Cambrosio and Peter Keating in *Exquisite Specificity*. It is in many respects a sordid tale of specious claims to priority, lawsuits and counter-suits, and distortions of science funding that do little credit to the scientific community, and even less to the biotechnology industry. The story is well told in this book.

If Köhler and Milstein had patented their finding, a great deal of grief might

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James Holmes/SPL

Culture club: 'sordid' tale of biotechnology uncovered.

have been avoided. It seems that the British patent office or the Medical Research Council turned down the idea because they did not find the discovery to be meritorious in this regard. Anonymous administrators responsible for such decisions should be publicly exposed for their bad judgement and incompetence. Perhaps the time has come to restore the stockades and gallows at Tyburn as a way of reintroducing accountability.

This history book should be of interest to the whole biology community. It is well illustrated to guide those not familiar with hybridoma technology through its details. Unfortunately the prose sometimes gets a little turgid. For example, try the sentence: "Explicitly or implicitly, to speak of a context is to reduce whatever is being contextualized to the elements that make up the context". In the foreword, Milstein quotes Jorge Luis Borges: "sólo quedan palabras. Palabras, palabras desplazadas y mutiladas" ("there remain only words. Words, displaced and mutilated words").

No exegesis on one of the most important discoveries of our century can diminish the lustre and impact of the paper by Köhler and Milstein. They were rewarded with the Nobel Prize for Physiology or Medicine in 1984. □

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Tunnel vision

I. Bernard Weinstein

Racing to the Beginning of the Road: The Search for the Origins of Cancer. By Robert A. Weinberg. *Harmony: 1996. Pp. 271. \$27.50.*

DURING the past few decades, our understanding of the origins of cancer has been tremendously enriched by the discovery of cellular oncogenes and tumour-suppressor genes. Robert Weinberg's book provides a nontechnical and exhilarating description of how this field evolved. The format is a series of anecdotes and stories laced with pungent descriptions of individual scientists, as well as examples of collaboration, bitter competition and a few cases of deliberate deception. These events are deftly woven together to illustrate the unpredictable nature of the scientific endeavour and how disparate areas of research can unexpectedly converge to provide new insights and models. Some of these stories are tedious, especially the lengthy descriptions of the research in Weinberg's own laboratory. But he did make important discoveries; this is his book, and he is not a modest man.

It is not apparent why, in glorifying the contributions of molecular biology to cancer research, the author finds it necessary to bash other disciplines, especially as the title of the book promises to take us "down the road", and not just one of the paths, in the search for the origins of cancer. For example, in an early chapter entitled "A can of worms" he states that by the 1960s the field of chemical carcinogenesis had reached an impasse and researchers in this field "became increasingly demoralized, seeing no clear way to advance their work". But for those of us who were there, this field was and still remains an exciting area of cancer research — and not because we are on Prozac.

Major discoveries were made, including the principles of metabolic activation and detoxification of carcinogens, the structures and mutagenicity of specific carcinogen-DNA adducts, the role of DNA repair as a host defence mechanism and basic principles of tumour promotion and hormonal carcinogenesis. These findings also provide profound insights into the origin of cancer, including the origin of specific mutations in *ras* oncogenes and the *p53* tumour-suppressor gene.

Weinberg glosses over these accomplishments by numerous investigators in the United Kingdom, the United States, Japan and elsewhere, and instead states that Bruce Ames's aphorism in 1979 that carcinogens are mutagens "had become the credo of our religion", even though in recent years Ames has backed away from this equation, recognizing that it is an over-