

Book Reviews

Several of the authors point out that while the origins of medical holism (as an oppositional movement) go back to the late nineteenth century, it attracted particular attention between the world wars. Although surprisingly few of them attempt to explain this renaissance, in aggregate these essays none the less tell us quite a lot about the conditions which fostered interwar holism. To begin with, the usual characterization of German holism—that it was mainly rooted in right-wing communitarian ideologies—is highly misleading. As Harrington's essay shows, Kurt Goldstein was on the liberal-left, and he was not alone. (Nor was holism elsewhere tied to communitarianism; in Britain, elite London clinicians championed an individualist political order.) Moreover, it is clear that the ideologized holism common in Germany was not typical of holisms elsewhere. In France and the United States, as Weisz and Brown make clear, holists largely stuck to medical evidence, without appropriating either general anti-reductionist arguments from biology or cultural criticism from the political arena. Nor were most medical holists in most countries concerned to link their arguments to wider anti-science movements.

If we are to account for the intensification of interwar holism, it is probably important to specify which kind of holism is to be explained. If we consider constitutionalist theories, for example, several authors suggest that one reason why they flourished in so many countries is that they could draw support, not only from the limited therapeutic successes of scientific medicine, but also from findings in immunology or eugenics which suggested that "soil" was as important as "seed". This argument is stated most forcefully by Mendelsohn, who argues that bacteriologists' experience of the peculiar properties of epidemics during and after the war made it very difficult to sustain the older view that the germ was all-important in disease. On the other hand, if we want to explain the ubiquity of clinicians' calls for an integrated knowledge of the body, then the prime candidate would seem to be Lawrence's thesis that clinicians' holism

was a response to the threatened reorganization of medical work after 1918.

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Scott H Podolsky, Alfred I Tauber, *The generation of diversity: clonal selection theory and the rise of molecular immunology*, Cambridge, Mass., and London, Harvard University Press, 1997, pp. x, 508, £49.95 (0-674-77181-8).

Several recent studies have shown the central role of techniques, instruments, reagents and experimental systems in the "molecularization of biology and medicine", first by focusing on the structure of proteins, then on the structure of nucleic acids (DNA and RNA). *The generation of diversity* is a fascinating account of how exactly this change took place in immunology. The book's main strength—telling a very detailed story of a transformation of a single domain of scientific inquiry—is probably also its most important drawback. Although Podolsky and Tauber systematically attempt to clarify and simplify the scientific problems they discuss, some of the chapters of their book may be unaccessible for a non-expert, a problem difficult to avoid when one deals with complicated scientific issues.

The generation of diversity focuses on debates about mechanisms which generate the diversity of antibodies. Briefly, the "dogma" of molecular biology has affirmed that an information concerning the synthesis of proteins flows exclusively from the nucleus (DNA) to the cytoplasm (synthesis of proteins), not the other way round. How can one account then for the fact that the body can produce specific antibodies (that is, protein molecules) which specifically react with a vast array of external antigens: not only pathogenic microorganisms, but also foreign proteins and even molecules produced in the laboratory? The answer for this puzzle was provided by the

clonal selection theory developed in the mid-1950s: the organism contains a large repertoire of antibody-producing cells, each synthesizing a slightly different protein molecule which is expressed on the cell's surface. The contact with a given antigen stimulates the proliferation (clonal selection) of cells which secrete antibodies able to react with that particular antigen. The clonal selection theory did not explain, however, how the body is able to produce the huge repertoire of pre-existing antibody molecules able to specifically react with all the possible antigens.

The search for the mechanism of the generation of diversity of antibodies occupied molecular immunologists for nearly three decades. The solution was provided by the molecular geneticist Susumu Tonegawa in 1984 (Tonegawa was honoured with the Nobel Prize for this study in 1987). To put it in a nutshell, Tonegawa demonstrated that the DNA segments which code for the variable parts of the antibody molecule (the parts which react with the antigen) are in fact composed from several independent genes which can combine in multiple ways. The result is that up to 18 billions of different antibodies can be formed from only 300 original genes. Tonegawa himself was not an immunologist, and he explained that he approached the question of antibody synthesis strictly as a genetic problem. He and his colleagues also affirmed that the main difficulty in explaining the generation of diversity was the development of an adequate conceptual framework. They stressed the differences between "germline theories" which proposed that there is specific gene coding for each individual antibody in the germline DNA, and the newer "somatic theories" which proposed that the diversity of antibodies is generated as a result of a combination of several genes. The development of "somatic theories" led to experiments which confirmed these theories.

Podolsky and Tauber contest this chronology. "Germline" and "somatic" theories, they affirm, co-existed in the 1970s. The main innovation introduced by Tonegawa and his colleagues was not conceptual but

methodological: the introduction of the molecular biology techniques. The widespread adoption of DNA methodology successfully blurred the differences (which were still important in the 1970s), between "cis" immunologists, concerned with cellular aspects of immunity, and "trans" immunologists, interested in the molecular structure of antibodies. In the 1990s immunologists, whatever their focus of study (including those who depart from the traditional perception of the immune system as a device allowing for self/nonself discrimination), have used essentially the same methods.

The study of the molecular aspects of immunology did not start, however, with the generalization of DNA technology. Two chapters of *The generation of diversity* are dedicated to the study of "molecular immunology" of the 1960s and 1970s, focused on protein structure. Podolsky and Tauber show the contribution of these studies to the understanding of the generation of diversity of antibodies. Later, however, the introduction of methods which directly investigated nucleic acids ("the recombinant revolution") led to a gradual abandonment of studies which focused on the structure of proteins, and then to their neglect. Descriptions of "crucial" experiments which demonstrated the rearrangements of segments of the antibody molecule were used later to establish the DNA technology as a critical arbiter of immunological theory. Research driven by the new technology, Podolsky and Tauber argue, changed the nature of immunological research, transforming this discipline from a cell-based science to one committed to the genome and molecular structure. Technology became a formative factor in the methodology of immunology and established not only the accepted practical ways to conduct research but also the theory how to conduct rational inquiry. From the mid-1980s on, DNA technology became a self-evident part of the immunologists' universe. *The generation of diversity* reminds us that this was not an ineluctable development. It could have been otherwise.

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