EUREKA! NEW IDEAS IN CELL BIOLOGY

The Society of Cells: Cancer and Control of Cell Proliferation. Carlos Sonnenschein and Ana M. Soto. Bios Scientific Publishers, Oxford, 1999. 168 pp. $34.95 (ISBN 0-387-91583-4 paper).

The historical record of science is punctuated by periods when iconoclastic personalities questioned fundamental assumptions and entrenched theories. Skepticism of the prevailing orthodoxy keeps science vibrant and responsive to new ways of interpreting natural phenomena. For example, in the seventeenth century, Galileo challenged the widely accepted Aristotelian principle that the weight of a body determined its time of free fall to the earth. Two centuries later, Ernst Mach dismissed Newton's ideas of absolute rest and absolute motion, arguing that all observations could be accounted for by a relativistic view of space and motion without having to posit "metaphysical fictions."

In that venerable tradition of reexamining entrenched ideas in science, the two authors of *The Society of Cells* have contributed a new theory of cell proliferation—one of the most challenging and enigmatic areas of modern biology. How do normal cells know when to stop dividing? Why do some cells proliferate in a culture medium but not in an intact plant or animal, and vice versa? Why do individual cells derived from neoplasms behave like normal cells?

Carlos Sonnenschein and Ana M. Soto begin their exploration by outlining the standard view of cell growth. In single-celled organisms, the default state is proliferation. Bacteria, yeast, and plant cells continue to reproduce as long as their nutritional requirements are met. However, animal cells, according to the standard view, have as their default state quiescence. According to this premise, cells will not proliferate in a nutrient-rich environment unless they are signaled to do so by growth factors. The authors ask why it is that throughout evolution, the constitutive property of proliferation for single-celled organisms and plants has been conserved whereas quiescence has emerged in animals.

To answer this question, the authors propose an alternative hypothesis that begins with the fundamental proposition that proliferation is the default state of all cells. This proposition, they argue, provides consistency between cell theory and evolutionary theory. It can also account for the incongruous data at least as well as the orthodox theory. Moreover, the authors note, "the notion that proliferation is the default state in all cells dispenses with the need to search for elusive positive signals" (p. 86) to explain why cells enter the cell cycle. Several chapters are devoted to a discussion of the methods and laboratory studies of cell growth, in which the authors provide side-by-side renderings of the standard hypothesis and their proposed alternative. To account for the fact that metazoan cells are not continuously proliferating, the authors introduce the concept of inhibitory factors of cell proliferation. They write that metazoan cells, like their single-celled progenitors, are always ready to proliferate unless prevented from doing so by a specific inhibitor(s).

Like many of their scientific forebears who have questioned orthodox theories, the authors describe a paradoxical result that turned their attention to a new way of thinking about cell proliferation. They discovered that certain cells that develop into estrogen-dependent tumors when inoculated into animals proliferate in culture at the same rate regardless of the addition of estrogens. When faced with experimental data that could not easily and elegantly be explained by the standard theory, Sonnenschein and Soto began rethinking the view that metazoan cells need a positive signal to proliferate.

The authors devote three chapters to examining the implications of their theory to the understanding of carcinogenesis. They then discuss the limitations of the somatic mutation theory of cancer and propose a bold new hypothesis that they call the "tissue organization field theory of carcinogenesis." According to this theory, neoplastic cells are considered "emergent phenomena resulting from a flawed interaction among cells and tissues." The authors dispute the idea that once a cancer cell, always a cancer cell. If this were true, they ask, "how can cells derived from these neoplasias revert to behave as normal cells?"

As Sonnenschein and Soto discuss, their theory has implications for cancer research. If carcinogenesis is a field phenomenon involving a disruption of cell–cell communication, then it must be studied at the level of tissues and organs. Studies of cells in culture, or what the authors call "carcinogenesis in a flask," investigate cancer at the wrong level of organization. The authors recognize the hurdles involved in maintaining cultures of tissues and organs to pursue the research program they advocate. But like the old story of searching in vain for the key under the lamp post because that is where the light is, the next breakthrough in the understanding of cancer may come from a shift in our basic assumptions rather than in new data.

This book is an honest examination of complex biological phenomena. It is written with clarity and modesty. The authors have ventured to do what few practicing scientists dare—namely, to reexamine the basic presuppositions of their field, subjecting the widely accepted beliefs that have nurtured even their own research grants to critical appraisal in the light of experimental findings. The eminent historian of science, Thomas Kuhn, noted that the growth of anomalies within a scientific paradigm is the spark that ignites new schemata for interpreting experiments and guiding research. *The Society of Cells* focuses attention on the anomalies of cell theory and carcinogenesis. In addition, it offers an alternative theory to account for the anomalies. Both the analysis of the anomalies and the new theory of cell proliferation deserve serious attention and discussion.

Historians and philosophers of science can read this book for its critical reflection on scientific orthodoxy. Practitioners of cell biology will find this work a formidable challenge to a field increasingly faced with ad hoc explanations that await a new synthesis.

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