Vasopressin: An Experimental Model

The Brattleboro Rat. Papers from a symposium, Hanover, N.H., Sept. 1981. HILDA WEYL SOKOL and HEINZ VALTIN, Eds. New York Academy of Sciences, New York, 1982. xx, 828 pp., illus. Cloth or paper, $150. Annals of the New York Academy of Sciences, vol. 394.

The discovery of the Brattleboro rat is a wonderful example of scientific serendipity. In 1961 Henry A. Schroeder, a retired associate professor of clinical physiology at Dartmouth Medical School, noticed that among his private colony of Long-Evans rats housed for research purposes in his summer home in West Brattleboro, Vermont, one cage always had an empty drinking bottle. This cage contained a mother and her litter of 17 pups. Schroeder and his assistant first determined that six of the pups were drinking excessive water and subsequently showed that this behavior could be reversed by treatment with the antidiuretic hormone, vasopressin. The Brattleboro rat was thus born, and the pups were then nurtured by Valtin and Sokol to become the Brattleboro strain at Dartmouth Medical School. The discovery of the rat is described by Valtin in the first paper in this volume, a compilation of 43 invited papers and 50 shorter research reports that were presented at an international symposium celebrating the 20th anniversary of the Brattleboro rat. About 120 scientists from four continents gathered to discuss the total biology of this mutant rat strain.

The principal interest in the Brattleboro rat is that it is unable to synthesize vasopressin and hence is valuable as an experimental model for diabetes insipidus. The mode of inheritance of the genetic defect is semirecessive (that is, the heterozygote has a vasopressin content intermediate between the homozygote and normals of the Long-Evans parent strain). Descendants of the original strain developed by Valtin and Sokol are now widely distributed and bred in laboratories all over the world. One of the major issues this book discusses is that these different laboratories have introduced the gene into diverse inbred rat stocks, thereby producing vasopressin-deficient rats with heterogeneous genetic backgrounds. This may be the cause of a number of discrepancies in the findings of different laboratories using the "Brattleboro rat," especially in studies that deal with highly complex phenomena related to vasopressin (such as behavioral studies). Therefore, the first part of the book, dealing with nomenclature, controls, reproduction, and development, is essential to anyone planning to use the Brattleboro rat for experimentation.

The book covers a wide range of experimental work in which the Brattleboro rat has served as a model and provides a great deal of information about the biochemistry and physiology of oxytocin and vasopressin. The book covers seven general subjects: reproduction and development, cell biology of the hormone-producing neuronal system (which includes anatomy, electrophysiology, and biosynthesis and secretion of the peptide hormones), electrolyte balance, hemodynamic mechanisms and hypertension, water balance and vasopressin receptor, endocrinopathies other than diabetes insipidus (such as interactions with the thyroxine and corticotropin systems), and disorders of behavior and the central nervous system. The papers are generally of high quality. Of particular importance are the paper by Valtin, which discusses the proper controls to use in experiments with the Brattleboro rat, and a panel discussion on reproduction and breeding. Papers by Morris and Dreifuss *et al.* discuss the anatomy and physiology, respectively, of the magnocellular neurons, which secrete vasopressin in normal animals, in the Brattleboro rat. It is intriguing that, except for the absence of hormone, related molecules, and secretory granules and an increased volume, these neurons are basically normal. The papers on electrolyte, water, and hemodynamic regulation are extensive and valuable. Also of interest is a paper by Gash and colleagues that describes an elegant use of the Brattleboro rat in neural transplantation studies. Unfortunately, the sequences of the vasopressin prohormone and the corticotropin-releasing factor (CRF) were published after this book went to press, and therefore the papers about vasopressin biosynthesis and CRF action, although useful, are out of date. In its molecular biological studies this field has lagged behind the other fields of endocrinology. This book simply reflects this fact. It is to be expected that study of the Brattleboro rat will soon employ the tools of molecular genetics to uncover the molecular nature of the genetic defect in this strain.

Perhaps of greatest interest to the general reader is the section of the book that deals with vasopressin and memory. In recent years, extrahypothalamic pathways of vasopressin-containing fibers have been described, and electrophysiological responses to vasopressin and oxytocin in the hippocampus and other areas of the brain have been found. Several papers in the book discuss these findings. It is possible that these pathways and receptors may be related to the reported effects of exogenous vasopressin on memory. The behavior of the Brattleboro rat is therefore highly relevant to this issue. The final section of the book contains a paper by Van Wimersma Greidanus that summarizes the experiments in which the Brattleboro rat has been used to show that vasopressin plays an important role in brain processes related to memory function. However, a variety of studies are presented in the book that oppose the thesis that vasopressin plays such a role. A lively discussion on this subject between the participants can be found at the end of the final section, although the reader cannot expect to find a resolution of the debate here. Indeed, the concluding comment in the discussion, "Maybe we didn't solve all the problems about the behavior and the behavioral performance of the Brattleboro rat," puts this field into proper perspective.

Taken as a whole, the volume is a well-balanced presentation of the subject and should be a useful resource book for anyone interested in neurohypophyseal peptide biology.

HAROLD GAINER
Laboratory of Developmental Neurobiology, National Institute of Child Health and Human Development, Bethesda, Maryland 20205

Cell Biology for Students

Molecular Biology of the Cell. BRUCE ALBERTS, DENNIS BRAY, JULIAN LEWIS, MARTIN RAFF, KEITH ROBERTS and JAMES D. WATSON. Garland, New York, 1983. xl, 1146 pp., illus., + index. $33.95.

Few fields of biomedical research have expanded as rapidly and as widely as cell biology. There can be little doubt that many of the very newest and hottest subjects of research, whether they involve immunology, genetics, or biotechnology, will be incorporated into this field. The expansion of subjects covered by cell biology and the vigorous production of knowledge create several major problems for anyone attempting to write a comprehensive and timely textbook in the field. The six authors of this stunning