Foreword

Imagine if you will a two or three day informal meeting in Emilia-Romagna, Italy, in which a group of scientists, mostly endocrinologists, with an admixture of immunologists, neuroscientists, mathematicians, theoretical biologists and philosophers of science have a chance to tell one another about their pet ideas, speculations, and cutting edge research into a wide variety of subjects. This meeting did not take place, but instead the editors of this fascinating volume have assembled an intellectual smorgasbord covering a vast array of topics, amounting, in fact to a virtual academia. Most of the authors are based in Italian Universities, or have Italian collaborators, but there is a liberal admixture of Americans and a sprinkling of scientists of other nationalities including the United Kingdom, Australia, Middle Europe, India, China and Russia, a variety of national backgrounds which mirror the broad range of topics covered by this volume.

Endocrinology receives the greatest attention, from articles in which the major problems are outlined in broad strokes, to others which provide in depth background discussion, and highly detailed data. Two new ideas about the cause and treatment of diabetes are proposed - the first that a recently described member of the tumor necrosis factor family of cytokines is mainly involved in damaging the islet cells in Type I diabetes, and the other that a neuropeptide, TRH, co-localized in pancreatic islet cells may exert a local protective effect, and conceivably could be a therapeutic agent. Also pertinent to the pathogenesis of diabetes is an elaborated hypothesis of the existence of a circulating factor derived from skeletal muscle, "the body's largest endocrine organ" which regulates pancreatic β cell mass. In the related area of insulin resistance syndrome, the genetic basis of tissue abnormality in familial lipodystrophy is proposed as a clue to the etiology of other forms of the disease. Another important area of cellular metabolism, apoptosis, is related to the actions of one or more "second messengers" such as 3'-phosphoinositol. Novel methods for studying cellular function have been developed using Carbon 13 detected in cells and extracts by Nuclear Magnetic Resonance measurements. In a speculative review of hypothalamic-pituitary control mechanisms, the case for a role of infundibular tanycytes in the neuroendocrine regulation of thyroid and gonadal function is convincingly made. These non-neural cells, which are intercalated with the nerve endings of the hypophysiotropic neuronal system possess a remarkable repertoire of biochemical functions, and morphological variation. One of the most provocative of the papers considers the problem of how to create a functioning thyroid gland taking into account the necessity for precise duplication of the normal topographical relatioships among thyrocytes, basement membranes, stroma and blood vessels.

Neatly segueing from Endocrinology to Immunology, the immunomodulatory effects of prolactin are reviewed, with special emphasis on its possible therapeutic effect in the human, and the pathogenesis of a rare autoimmune disease that causes polyendocrinopathy, candidiasis and ectodermal dystrophy is considered. The genetic abnormality is in a particular regulator gene, but the specific cause of pituitary damage may be cross reactivity of an anti-candida enolase antibody with an enolase in pituitary cells. And in a segue to neuroendocrineimmunology, a detailed account is given of the mechanisms by which the peripheral immune response is sensed by the central nervous system, and how this central response triggers the characteristic endocrine response to peripheral inflammation.

Brand new techniques arising from genetics and proteomics have led to exciting new empirical approaches to cancer diagnosis. The capacity to identify literally hundreds of unique proteins present only in trace amounts in human blood have led to the recognition of unique patterns with high value in the early diagnosis of thyroid cancer. These methods are applicable to the entire spectrum of cancer, and can serve in both diagnosis and monitoring of therapy, and in the search for new therapeutic methods.

All of the foregoing papers follow a relatively traditional approach to research in which a problem is identified, hypotheses defined, and experimental study carried out. The next group of papers are not as easily pigeonholed, but all have a mathematical or formal logical approach. The theoretical, computational and mathematical aspects common to spatial imaging is considered in a theoretical way and then applied to the understanding of imaging technology, which has revolutionized diagnosis and understanding of pathophysiology of disease. The most advanced papers in this collection deal with the most difficult of contemporary problems in neuroscience - the brain as a computer, the limits of applying theoretical mathematics to understanding consciousness, cognition, and execu-

tion. How mechanistic changes in neuronal function could account for learning and memory is also considered.

Two totally provocative papers in this collection, and completely outside the main stream of current cellular theory is a novel approach to understanding anatomical organization of the body based on the structure of the supporting matrix, and analogizes biological function with more general properties of crystals.

And finally, one of the authors takes on an almost impossible challenge. In one fell swoop he considers how rational man, from the dawn of history has learned how to identify and abstract the *nature* of knowledge derived from observation of the external world and purely intellectual, i.e. inner derived analyses.

The collection of papers presented in this volume cover a uniquely large range of scientific and formal logical questions in modern biology. It presents the challenge of how one integrates knowledge in a world of exponentially expanding information.

Seymour Reichlin, M.D., Ph.D.
Emeritus Professor of Medicine
Tufts University School of Medicine
Boston, MA, USA