Preface

In 1986, my laboratory was searching for transcription factors that might control the activation of the kappa immunoglobulin light chain when we came across NF-κB. We thought it was specific to B-lymphocytes and never imagined that it would turn out to be among the most protean of transcription factors ever discovered. But that realization came during the next few years as we first found that it could be induced in many cells and then found that it was stored in the cytoplasm, ready to be activated by a wide range of inducing stimuli. When its sequence was first determined, we realized that it had a history before 1986; Howard Temin's laboratory had discovered the Rel oncogene years before and it is a slightly altered member of the NF-κB family of proteins.

This book contains much that is known about the basic biology of NF-κB or at least references to it. Its clearest function is as a transcription factor orchestrating the activation and repression of many genes involved in inflammation, but it also helps activate genes of innate and adaptive immunity in response to pathogens, maintains liver integrity in the developing mouse, plays multiple roles in the nervous system, and is implicated in skin, hair, and tooth formation and much more in the vertebrate body. In insects, homologues of the mammalian proteins are involved in defense against pathogens but also play key roles in development (for example, *dorsal* in *Drosophila* establishes dorsal/ventral polarity in the developing embryo).

Any system in the body that plays so many important roles is likely to also cause pathology when it goes awry, and NF-κB is no exception. Its role as an oncogene showed early on that it could be a cause of cancer, and the linkage of cancer and inflammation, which is so widely discussed today, is another reason for linking NF-κB to cancer induction. NF-κB is implicated in a wide range of other pathologies, including heart disease, muscular dystrophy, and many other conditions involving chronic inflammation.

In 1986, we knew only a few transcription factors and only a few of the intracellular proteins that transduce signals from cell surface receptors. Today, we stare at myriads of components whose interactions make urban subway systems look simple. A remarkable fraction of these intracellular mediators are parts of pathways that lead to or through NF-κB. Thus, what was supposed to be a simple regulator of a particular step in differentiation has turned out to be linked by transduction pathways to many of the cellular signaling pathways. This book then is one of many that should be read together if the full richness of the cell's transduction machinery is to be understood. No one person can today absorb this body of knowledge and no one can keep pace with its continued growth. But each member of the community of interested scientists must absorb what she or he can and then share in the interactions that bring together the joint knowledge that one day will describe all of cellular metabolism. Because new students interested in these systems are

continually entering the field, a book such as this is an entry point for them, and it is to these newcomers that I dedicate this limited preface.

David Baltimore