Preface

Fibroblast growth factor family is the largest and most diverse group of growth factors involved in many aspects of normal biology and disease pathogenesis. FGFs have the additional distinction of being the first growth factors identified. Although FGF2 (basic FGF), the first FGF to be purified, was originally isolated from the bovine pituitary extract based on its ability to stimulate proliferation of BALB/c 3T3 fibroblasts, subsequent studies showed a very broad expression pattern. Similarly, FGF1 (acidic FGF), while initially isolated based on its ability to stimulate growth of endothelial cells, was subsequently shown to also act on a broad spectrum of cells. Subsequent studies using heparin sepharose chomatography and molecular cloning greatly expanded the size and diversity of the FGF family.

The FGF family of ligands and the corresponding family of FGF receptor tyrosine kinases comprise one of the most versatile and diverse growth factor signaling families in vertebrates, playing critical roles in a wide variety of biological processes. In addition to the twenty-two FGF ligands and four tyrosine kinase receptors, there is a number of co-receptors and cell-surface and cytoplasmic proteins that modulate FGF signaling in a tissue and cell-type specific manner. This great diversity and complexity of FGF biology is at the core of the multitude of biological activities and role ascribed to these growth factors.

Recent years have seen major expansion of knowledge about this family of proteins and it would be impossible to cover all aspects of their biology with any degree of completeness. For that reason

this monograph is focused largely on vascular effects of FGFs. This choice is motivated, in part, by recent advances in our understanding of FGFs' role in the vasculature and by the growing understanding of vasculature's contribution to the regulation of normal organ homeostasis as well as better appreciation of the role of abnormal FGF singaling in a wide array of disease processes. With this focus in mind, we explore everything from the structure and signaling of FGFs and their receptors (Chapters 1, 2 and 3) to their role in the regulation of vascular homeostasis (Chapter 4) to their role in cardiovascular diseases (Chapters 5 and 6). We then address new developments in FGF therapeutics (Chapter 7) and explore FGF biology in the epithelium (Chapter 8) thereby providing a complete analysis of this growth factor family biology in two closely related but distinctly different environments- endothelium and epithelium. Finally, we examine FGF biology in eye disease and in cancer.

It is our hope that this comprehensive treatment of FGF vascular biology and its application will provide the reader with the accurate and timely summary of this rapidly moving field.