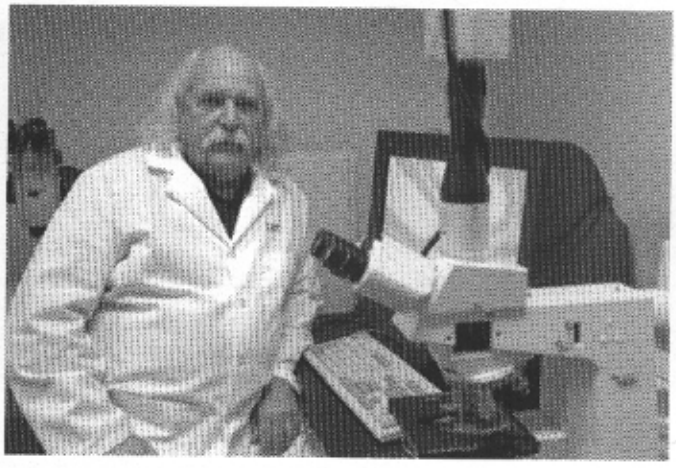
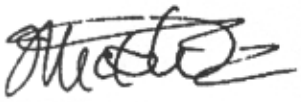
Preface



In 1974, Gospodarowicz, Jones, and Sato reported the presence of a growth factor for ovarian cells in extracts of pituitary that was subsequently named fibroblast growth factor (FGF) because of its potent mitogenic activity on fibroblasts. The finding led to a potent and essentially ubiquitous tyrosine kinase cell signaling family that is now comprised of 18 receptor-mediated FGF polypeptides and four homologues and a myriad of splice variants from four receptor genes controlled by cofactors heparin sulfate and klothos. As members of the signaling family grew, it became apparent that there is unlikely a tissue or biological process where one or more members are not present and at play, attracting a growing field of diverse biologists studying details of structure-function to clinical applications. FGF family signaling plays a key role in embryonic development, adult tissue homeostasis and metabolism and its dysfunction, which are of potential importance in related diseases.

Chinese scholars have contributed significantly to our knowledge about the FGF family. Dr. Xiaokun Li was among the first to study FGF in China and has been a driving force in development, application, and education in the FGF-signaling field within China and also worldwide. Advancing the field of FGF signaling and its applications for medical treatments are his personal passion. I have been fortunate to personally witness Dr. Li's work since attending the third International Conference on Fibroblast Growth Factors at Wenzhou, which he hosted. The conference brought together interests from across China and the world.

This book is a collection of research results from Dr. Li's group, spanning application of engineered nonmitogenic mutants, structure modification, pathology, physiology, pharmacology, FGF/FGFR (receptor) inhibitors, bioengineering and drug development to injury repair and regeneration as well as other biological processes. This work should be a helpful primer to scientists and particularly students entering the FGF field with their eye toward applications.



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Historically speaking, fibroblast growth factor (FGF) signaling as a research field was conceived in the late 1930s/early 1940s by the observation that bovine pituitary extracts contain mitogenic factors for fibroblast cell lines. Some 30 years later, these mitogens were purified and characterized as FGF1 and FGF2, the founding members of the FGF family. An additional seven FGFs were then discovered either as oncogenes or mitogens using classical functional and biochemical methods and then genomic research added nine more FGFs. The FGF family stands today as one of the largest growth factor families in humans, consisting of 18 members in mammals. Gene knockout in animal models and clinical studies in human patients have attributed pleiotropic functions to FGF family in mammalian development, tissue homeostasis, and metabolism. FGF ligands signal in paracrine and endocrine fashion through four cell-surface FGF receptor (FGFR1-FGFR4) tyrosine kinases and their multiple alternatively spliced isoforms. Ligand binding induces FGFR dimerization enabling tyrosine transphosphorylation of intracellular receptor kinase domains and hence kinase activation. For two decades, several mitogenic, cytoprotective, and angiogenic therapeutic applications of paracrine FGFs have been explored worldwide, and the recent discoveries of the key roles of the endocrine FGFs in energy and mineral homeostasis have expanded the pharmacological potentials of this family. Alongside laboratories in the United States and Western Europe, several Chinese research laboratories have also made valuable contributions to the clinical development of the FGF family. Notably, Xiaokun Li's group at the Wenzhou Medical College specializes in state-of-art

technologies to discover novel FGF-based therapeutics for tissue repair, regeneration, and metabolic disorders. His research efforts has resulted in three A-grade FGF-based drugs and one FGF-containing collagen sponge that have been approved by China SFDA for wound healing and skin repair. This book gives an overview of the basic and applied research conducted in the Xiaokun Li's laboratory and is highly recommended to graduate students and researchers in the FGF field.

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