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Preface

# TGF-β signaling in development and disease

The articles assembled in this especial issue of FEBS Letters review current progress and perspectives on various aspects of transforming growth factor β (TGF-β) signaling in development and disease. A flood of new information emerging at the FASEB Conference on the TGF-β Superfamily, in August 2011, provided impetus for this review series. The new work emphasizes key aspects of the core TGF-β signaling pathway that had long remained obscure. The TGF-β family was identified in the early to mid 1980s, and their basic signal transduction mechanism came to light in the mid 1990s. Building on those pioneer findings, many groups set out to explore the role of this pathway in virtually every major step of embryogenesis from stem cell differentiation to body axis formation and the morphogenesis of tissues and organs. In parallel, an unrelenting effort defined the role of the TGF-β family in the homeostasis of epithelial and endothelial tissues, hematopoietic and immune systems, and skeletal and neural organs. Virtually all cell types were found contain an active TGF-β system regulating cell fate, proliferation, movement, polarity, adhesion, cytokine production, modification of the microenvironment, terminal differentiation and cell death. As the prominence of this pathway became increasingly clear, so did the realization that many aspects of the TGF-β signal transduction process remained inadequately understood. The present set of review articles covers recent progress in recognizing and elucidating these important gaps of knowledge.

Wylie Vale and Peter Gray describe the versatile role of cripto co-receptor molecules in controlling the access of TGF-β family members to signaling receptors. Yoav Henis and his colleagues offer their views on the oligomeric interactions between the receptor components in the TGF-β and bone morphogenetic protein (BMP) systems. Thomas Mueller and Joachim Nickel review the determinants of specificity of BMP receptors. Additional perspectives on TGF-β receptors are provided by Andrew Hinck and Rik Derynck. Moving one step further in the pathway, Gopal Sapkota reviews the regulation of Smad transcription factors by phosphorylation at the core of the canonical TGF-β signal transduction pathway. Stuart Newfeld discusses the roles of mono- and poly-ubiquitylation of Smad in TGF-β and BMP signaling. Akiko Hata reviews the unexpected role of Smad proteins in micro-RNAs biosynthesis. Xuedong Liu discusses the dynamics of TGF-β driven Smad signaling. On a more global scale, Caroline Hill offers perspective on the spatial regulation of BMP signaling in mammalian cells, and Laurel Raftery writes on the quantitative imaging of this process in Drosophila.

Moving on to development and disease, Qiaoran Xi and I review how Smads interface with the chromatin of differentiation genes in embryonic stem cells. In their respective articles, Kunxin Luo and Shirin Bonni discuss the roles of the Smad regulator SnoN in embryonic development and in post-mitotic neurons, respectively. Carl Heldin and Aris Moustakas provide an insightful perspective on the role of TGF-β in epithelial-mesenchymal transitions (EMT) in development and cancer. Xiao-Jin Wang focuses on Smad4 loss-of-function as a mediator of tumor initiation in head-and-neck cancer and tumor progression in pancreatic cancer. Perter ten Dijke focuses on the role of BMP signaling in the cardiovascular system and its disorders. Harold Dietz and Jeffrey Doyle discuss genetic disorders that perturb the interaction of TGF-β and the extracellular matrix, with grave consequences. Alain Mauviel reviews recent findings on the crosstalk between the Hedgehog and TGF-β pathways and its implications in cancer.

In a separate note, Peter Gray and I celebrate the life and key contributions of Wylie Vale, who sadly passed away as the present work was going to press. This issue of FEBS Letters is dedicated in memory of Wylie Vale.

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