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EDITORIAL

IGFBP special issue – introduction

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This issue of Journal of Cell Communication and Signaling is devoted to papers on the insulin-like growth factor binding proteins (IGFBPs). The six IGFBP genes found in mammals are part of an evolutionarily complex family, in which the number of genes ranges from 5 in some avian species to up to 11 in fish (Daza et al. 2011). Common features of the IGFBPs include conserved cysteine-rich amino- and carboxyterminal domains, and a structurally diverse central or linker domain. The aminoterminal domain includes the so-called IGFBP motif GCGCCXXC which is also found in proteins of the CCN family, named for its members Cyr61 (CCN1), CTGF (CCN2), and Nov (CCN3). The carboxyterminal domain largely consists of a single thyroglobulin type-1 repeat, which includes a highly basic sequence with functional activity as a nuclear localization signal in some IGFBPs. The IGFBPs are distinguished from other proteins that include these domains, by their high-affinity binding of the insulin-like growth factors IGF-I and IGF-II.

While the transport of IGFs in the circulation, and their delivery to tissues, are undoubtedly central roles of the IGFBPs, increasing attention is being paid to their cellular functions which, in many cases, appear unrelated to their IGF-binding activity, and can be demonstrated even in IGFBP mutants with greatly attenuated IGF affinity. This special issue focuses principally on pericellular and intracellular IGFBP actions, both IGF-dependent and -independent. In terms of disease focus, the papers concern IGFBP function in both cancer and metabolic disease, the two most widely-studied areas of IGFBP action. Among post-translational modifications of IGFBPs that are known to modulate their activity, phosphorylation and limited proteolysis have been most extensively studied at the mechanistic level, and two papers, by Gupta and Oxvig, discuss novel aspects of IGFBP-1 phosphorylation, and IGFBP-4 proteolysis, respectively, as important regulatory mechanisms. IGFBP-2 is examined for its roles in metabolic regulation (Wiedmer et al.) and cancer (Yau et al., Beattie et al.), the latter paper also concerned with IGFBP-5, especially in the mammary gland. Perks and Holly review the epigenetic regulation of IGFBP-3 in the cancer context, and the article by Chua et al. covers novel aspects of IGFBP-3 and other IGFBP activity in the DNA damage response. Finally, newly-discovered IGF-independent actions of IGFBP-6 are discussed by Bach.

This IGFBP issue represents a unique accumulation of contemporary thought on IGFBP actions from several leading laboratories in this area. Despite major advances in our understanding of the diverse roles of the IGFBPs, there are still many unanswered questions — indeed, the gap between in vitro discoveries and their applicability in vivo to improve human health or animal production has never seemed wider. Thus it is hoped that this issue will prompt further enquiry into this important family of proteins, and that the resulting expansion of knowledge may be translated for wide benefit.

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Reference

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