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Mechanism of signaling via TGF β receptors

Our aim is to elucidate molecular mechanisms involved in TGF β signaling in normal and malignant cells. TGF β has both tumor suppressor (inhibits growth and induces apoptosis) and tumor promoting (stimulates invasiveness and metastasis) effects in cancer cells. In addition, TGF β exerts pro-tumorigenic effects in the tumor micro-environment, since it stimulates angiogenesis and the development of cancer associated fibroblasts, and inhibits immune surveillance. TGF β binding to type I and type II receptors (T β RI and T β RII, respectively), induces signaling via Smad transcription factors which affects the transcription of specific genes, as well as via non-Smad pathways, including MAP-kinases, PI3-kinase, the tyrosine kinase Src, and liberation of its own intracellular domain (ICD). We are interested in elucidating the mechanism by which TGF β induces pro-tumorigenic and tumor suppressive pathways. Our goal is to develop selective TGF β inhibitors which inhibits the pro-tumorigenic pathways, while leaving the tumor suppressive pathways unperturbed.

