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Effects of Extracellular Transforming Growth Factor-mediated Fibroblast Activation in Tumor Microenvironment[1] ROBERT DILLON, ADNAN MORSHED, PRASHANTA DUTTA, Washington State University — The transforming growth factor (TGF) is known to prevent differentiation of benign tumor cells to malignancy. Paradoxically, cancer cells exploit the immune regulation and microenvironment modulatory functions of TGF to their advantage. This makes TGF response highly sensitive to tumor progression. In vitro experimental data for several intercellular and cell surface reactions involving the fibroblasts indicate a switch-like behavior based on extracellular TGF conditions. We modeled a single tumor cell with surrounding fibroblasts to create a specific tumor microenvironment. The extracellular transport through advection, reaction and diffusion as well as cell surface reactions are captured through an immersed interface approach. Flow of extracellular nutrients and fluid-structure interactions are modeled with an immersed boundary description. The unknown reaction parameters were estimated using Bayesian inference with experimental data on the PE25 cell line. Variation in spatial distance and arrangement of tumor cells and fibroblasts showed significant change in reaction dynamics and intracellular TGF production. Microfluidic results also highlight the clinical relevance and therapeutic potential of TGF/Smad pathway.

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