Tumors show increased tissue level forces and a present with a chronically stiffened extracellular matrix (ECM), and transformed cells exhibit a perturbed oncogene-stimulated and ECM-tuned mechanophenotype. We have been studying how these aberrant cell and tissue level forces promote malignant transformation and drive tumor metastasis, and how they modulate tumor recurrence and treatment resistance in breast and pancreatic cancer and glioblastoma. We use two and three dimensional culture models with tuned extracellular matrix stiffness, as well as transgenic and syngeneic mouse models, human PDX models and human biospecimens, in which ECM crosslinking and stiffness and integrin mechanosignaling can be quantified and modified. Our studies have thus far revealed that the ECM in all tumors is progressively remodeled and stiffened by stromal fibroblasts and that this occurs prior to malignant transformation. We determined that ECM remodeling and stiffening is mediated very early during malignancy by stromal fibroblasts that are activated by factors including TGFβ that are secreted by infiltrating pro-inflammatory macrophages. The stromal-fibroblast stiffened ECM disrupts tissue organization, promotes cell growth and survival and drives cell invasion. A chronically stiffened tissue stroma drives angiogenesis, and activates STAT3 to induce key cytokines and chemokines that promote pro-tumor immunity to foster tumor growth and dissemination and impede tumor treatment. The stiffened ECM also drives an epithelial to mesenchymal transition and primes the metastatic niche to foster metastasis. I will discuss the dynamic and reciprocal interplay between tissue tension and innate and acquired immunity and how this can not only force tumor aggression and metastasis but may also initiate tumor progression.