

## Cellular plasticity within the tumor ecosystem: heterotypic models to interrogate tumor and tumor microenvironment interactions

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As tumors develop, coordinated changes to cell state occur not only in tumor cells, but also in cells of the tumor microenvironment. Expression of oncogenic mutations in epithelial cells can induce plasticity toward a premalignant state, but this alone is often not sufficient for tumor development. In many cases, additional environmental changes (e.g. inflammation) are necessary to allow for a premalignant to malignant transition. A major question in the field, therefore, is whether tissue environments can be controlled in order to suppress tumor development. Addressing this, however, requires a mechanistic understanding of cellular plasticity and the dynamic and reciprocal interactions between multiple cell types. I will present examples of the heterogeneity and plasticity of both cancer and tumor microenvironmental cell types in response to extrinsic/environmental signals, and discuss approaches to building complex, heterotypic in vitro models to test the plasticity of cell states and cell behavior in the tumor ecosystem.