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Role of Epithelial-Mesenchymal Transition in Tumor Progression

The EMT program plays a key role in the malignant progression of carcinoma cells of various types. Indeed, it is increasingly plausible that blockage of activation of versions of this program can prevent invasion and metastatic dissemination of the neoplastic cells in primary carcinomas. As more detailed characterizations of this program appear from various laboratories, it appears that the EMT program is rarely if ever driven to completion in spontaneously arising carcinomas. Instead, initially epithelial cells advance part-way through this program, acquiring mesenchymal attributes while retaining certain epithelial ones. Resulting cells of mixed epithelial-mesenchymal phenotype appear to harbor subpopulations of tumor-initiating cancer stem cells. The derivation of more epithelial and more mesenchymal carcinoma cells from the MMTV-PyMT model of adenocarcinoma pathogenesis has made it possible to assess the relative contributions of these two cell types to interactions with the immune system. This has led to the demonstration that epithelial carcinoma cells are relatively susceptible whereas more mesenchymal counterparts more resistant to elimination by checkpoint immunotherapy. Moreover, minority subpopulations of mesenchymal carcinoma cells are able to protect coexisting majority subpopulations of more epithelial counterparts within the same tumor from elimination by checkpoint immunotherapy. These dynamics would seem to hold important implications for predicting the responsiveness of various carcinomas to such immunotherapy.