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Countering tumor progression by targeting of a driver of the epithelial-mesenchymal transition

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The epithelial-mesenchymal transition (EMT) constitutes a relevant process during the progression of carcinomas, as it mediates the conversion of stationary, epithelial tumor cells into mesenchymal-like, invasive cancer cells. We recently identified the T-box transcription factor brachyury, a molecule predominantly expressed in human tumors but only rarely expressed in normal adult tissues, as a novel driver of the EMT process in human carcinoma cells. Brachyury was demonstrated to induce the expression of molecules associated with the mesenchymal phenotype, human tumor cell motility and invasiveness in vitro, as well as metastatic propensity in xenograft models. Analysis of expression in multiple human tumor tissues demonstrated a preferential expression of Brachyury in higher stage lung tumors, suggestive of a role of Brachyury in human lung cancer progression. Analysis of breast cancer tissues also revealed expression of Brachyury in primary breast tumor samples as well as in 100% of breast cancer metastatic lesions analyzed by immunohistochemistry. We have now shown a positive correlation between Brachyury expression in epithelial tumor cells and features of tumor stemness, including resistance in response to treatment with various chemotherapeutic agents or radiation. In search for an approach to target tumor cells with high levels of brachyury, we have characterized its immunogenicity and developed brachyury-based cancer vaccine platforms, one of which is currently undergoing Phase I clinical testing. We hypothesize that the eradication of brachyury-expressing tumor cells via immunotherapeutic approaches could be efficient at eliminating tumor cells with invasive/metastatic potential as well as tumor resistance to conventional therapies.

Biography

Claudia Palena is an Investigator and the Head of the Immunoregulation Group in the Laboratory of Tumor Immunology and Biology, National Cancer Institute, NIH, Bethesda. She received her PhD degree in Biochemistry from the National University of Rosario, Rosario, Argentina, in 2000, and subsequently completed a Postdoctoral Fellowship in the Laboratory of Tumor Immunology and Biology, NCI. She has published extensively in the area of human tumor antigen discovery and cancer vaccines. Her current research is focused on the development of novel immunotherapeutic approaches aimed at targeting critical events in tumor progression with the ultimate goal of designing vaccine(s) platform(s) and combinatorial therapies for the prevention and/or treatment of metastases in human cancer.

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