

## Bankhead-Coley Cancer Research Program

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*2009 Program  
New Investigator (3-year project)*

**Project Title:** Mechanisms of Tumor-Induced Local Immunosuppression

**Project Summary:** Advances in cellular and molecular immunology have brought various concepts and ideas to cancer immunology, leading to breakthroughs in cancer immunotherapies that are being tested in an expansion of clinical trials. These trials have generated promising results that may lead to the goal of curing cancers, but have also revealed many challenges that are difficult to address. As exemplified in cancer immunotherapy trials by blocking the cytotoxic T lymphocyte antigen 4 (CTLA4), a prominent issue that has emerged is the entangling of autoimmunity toxicity and antitumor immunity. We propose to use new mouse models to dissect the autoimmunity implications in antitumor immunity. Our focus is on the quantitative interactions among CTLA4, regulatory T (Treg) cells, and the tryptophan-degrading enzyme indoleamine 2,3-dioxygenase (IDO) since these elements may present a major hurdle for immune destruction of tumors. The quantitative variation of CTLA4 is associated with human autoimmunity, cancer occurrence, and both the autoimmune toxicity and therapeutic efficacy in cancer immunotherapy. A better understanding of the CTLA4-mediated local immunosuppressive mechanisms at the tumor site will help therapeutic targeting to overcome the local immunosuppression at the tumor sites while minimizing off-target autoimmune adverse effect.