

Bankhead-Coley Cancer Research Program

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*Gastroenterology and Hepatology
University of Florida*

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

Project Title: Regulatory Immunologic Mechanisms in Hepatocellular Carcinoma

Project Summary: Liver cancer (HCC) is the fifth most common cancer worldwide, and the fastest growing GI malignancy. The majority of patients with HCC present in the latter stages of the disease and conventional chemotherapy has failed to impact survival. As such, new treatment strategies are urgently needed. Our preliminary studies have shown that patients with HCC have ineffective immune responses, which are characterized by elevation of suppressive CD4+CD25+ regulatory T cells (Treg), poor effector T cell (Teff) responses, and significant elevations in soluble CD25 (sCD25). The impaired Teff responses, elevated Treg frequency, and higher levels of sCD25 correlate with tumor stage and patient survival. This grant consists of two specific aims that explore the hypothesis that HCC promotes the release of sCD25, which impairs tumor immunity by suppressing Teff responses and enhancing Tregs, thereby promoting HCC development and progression. Aim 1 determines the cellular sources of sCD25 and seeks to identify a functional role for sCD25 on Teff responses as well as Treg function. Aim 2 directly evaluates the immune profile of HCC patients (sCD25 level, Teff response, and Treg frequency) as novel immune biomarkers that correlate with prognosis and treatment response. This grant is designed to increase the cancer research capacity for patients with HCC by identifying novel prognostic and treatment monitoring tools as well as targets for immune-based therapy.