

## Bankhead-Coley Cancer Research Program

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*2010 Program  
New Investigator Research  
(3-year project)*

**Project Title:** The Role of Smoking in Promotion of Crohn's Disease, a Predisposing Condition to Colon Cancer

**Project Summary:** Smoking is implicated in many diseases other than lung cancer. For example, smokers are at a higher risk for developing and dying from colon cancer, and are more likely to develop Crohn's disease (CD), a chronic inflammatory condition of the colon. CD alone is a risk factor for colon cancer. Therefore, smoking triggers inflammation, and this inflammation is conducive to the development of CD and cancer. However, the underlying mechanisms for these events are unclear. Mutation of the gene ATG16 is a risk factor for CD. ATG16 is essential to autophagy, a process that kills bacteria. When ATG16 is mutated, our cells kill bacteria less well, and resulting bacterial persistence promotes inflammation. Persons with mutant ATG16 are ~8 times more likely to have CD if they smoke, but whether their disease is more severe is unknown. We propose that smokers with mutant ATG16 will have more severe CD, and we will study this by reviewing their medical and smoking histories. Next, we propose that white blood cells (WBC) are negatively affected by smoking and ATG16. We will study this by measuring bacterial killing and inflammatory chemicals from WBC in these patients. This work is important because it will aid our understanding of how behavior and genes interact to alter our risk for CD and cancer, and will allow for improved risk-stratification and patient care.