

Bankhead-Coley Cancer Research Program

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Medicine
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Florida Research Challenge
(2-year project)

Project Title: The Role of PKR in Chronic Inflammation and Leukemogenesis

Project Summary: Inflammation is the process by which chemicals and cells from the body's immune system are released into the blood and circulate to affected tissue in response to infectious or other foreign agents. Prolonged inflammation, or chronic inflammation, arises when the immune response is not completely shut off due to persistent stress like cigarette smoke or certain infections. By affecting the interaction between cells and their surrounding environment, chronic inflammation plays an important role in driving tumor formation. To better understand the mechanism by which chronic inflammation can promote cancer, we are developing two novel mouse models. These mice will express specifically in blood and immune system cells either increased amounts of the gene Pkr or a mutant nonfunctional form of Pkr. Since, the PKR protein is a critical activator of inflammatory systems and cell death, we expect that mice with increased PKR will be prone to bone marrow failure disorders and preleukemias including Myelodysplastic Syndrome or aplastic anemia. In contrast, mice expressing mutant, nonfunctional PKR are expected to have bone marrow cells resistant to death and the development of leukemia. Importantly, these studies are expected to provide valuable new insights into how chronic inflammation can cause cancer and may in the future lead to the development of novel anti-cancer agents targeting PKR-driven inflammation.