John M. Cunningham, MD - 2010 Fletcher Scholar

"Characterization of the nuclear architecture of leukemia stem cells"
2011 Interim Report

I was funded through this award to focus on two complementary areas. In specific aim 1, we proposed to develop a comprehensive understanding of the histone code and its distribution in normal blood stem cells and malignant leukemia stem cells. Achieving this goal is likely to not only provide insights into the biology and prognosis of therapy related or t-AML, but also identify novel therapeutic targets.

To reach our goal, we have established the central assays including ChIP-Seq and FAIRE. This has required bringing together biochemists and bioinformaticists, and using leukemic cell lines as models. We are currently validating our results, which appear very informative. We are now poised to use these assays to address the same questions in primary hematopoietic stem cells and their leukemic counterparts derived from patients. We expect to have significant results in the next six months in this area. This goal is facilitated by the coincident establishment of a mouse model of human leukemia as a source of cells.

In a second area, we proposed to explore a second area, the divergent roles of distinct sub-nuclear compartments in leukemic transformation and maintenance. This has been a more challenging endeavor, and we have focused all our efforts on Specific Aim 1 this year. I expect that with the recruitment of a new post-doctoral fellow to the laboratory, that we can make significant progress on this goal in the coming year.

In summary, the funding of the Fletcher award has been instrumental in 'jump-starting" this aspect of the larger t-AML award. I am personally grateful for your support, and look forward to providing clear and exciting results that advance our understanding of t-AML and its treatment at my next report.