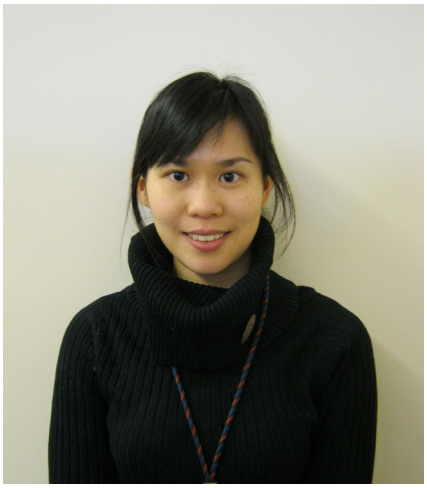
Congratulations to Vionnie Yu, Ph.D., 2010 recipient of the Bullock-Wellman Fellowship!



Project title:

Defining the stromal contribution to leukemia development using a multi-fluorescent transgenic model

Project Abstract:

The bone marrow microenvironment consists of a variety of support cells for hematopoietic stem cell maintenance, including osteoblasts, pericytes, endothelial cells, and mesenchymal stem cells, may also serve as a critical participant in leukemia development by providing essential elements for the survival of cancer cells. Studies targeting the microenvironment showed promises in sensitizing leukemic cells to cytotoxic agents and suggest that the interaction of bone marrow stromal cell and leukemic cell enforces the survival of the malignant cells. Our laboratory has previously defined the endosteal niche that hosts normal hematopoietic stem cell[3] and demonstrated the important role of osteoblast in regulation of hematopoietc stem cell quiescence and self-renewal. However, the existence of a leukemic niche and the specific components of the niche that contribute to hematologic malignancy are currently unknown. I propose to explore the microenviromental contribution to acute myeloid leukemia development by tracing the clonal contribution of mesenchymal subtypes *in vivo* during leukemogenesis using a multi-fluorescent transgenic mouse model (Rainbow). Using Rainbow mice, individual mesenchymal cell will be labeled endogenously with a unique fluorescence such that clonal expansion of an individual cell to its respective descendents can be followed. Such animal model allows *in vivo* investigation of whether there is preferential expansion or distribution of specific niche cells that mediates leukemic development. Secondly, I will assess the therapeutic effect of endogenously deleting such specific cell population in altering disease outcome in a murine leukemia model. I have created a constellation of genetically engineered mice to perform both lineage tracing and selective cell depletion experiments to define fundamental characteristics of these cells *in vivo*. If successful, these studies will determine whether a specific mesenchymal subtype is a cell population to target in developing treatment for leukemia while conserving the normal hematopoietic stem cell counterpart.

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