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Bio500 abstract

Research Abstract:
The main interest of our laboratory is the discovery and characterization of gene mutations in patients with myelodysplastic syndrome (MDS) with the long term goal of understanding the molecular mechanisms that control abnormal hematopoiesis. MDS results from the expansion of one or more dominant hematopoietic clones that contain initiating mutations, while transformation from MDS to acute myeloid leukemia (AML) occurs as these clones accumulate additional progression factors (including point mutations in genes and cytogenetic abnormalities).

Current projects include the following:

Whole genome sequencing
Gene mutations are identified in the genomes of hematopoietic cells from patients with MDS and AML using next generation sequencing technology. Somatic mutations are also used to decipher the clonal architecture of MDS and AML samples. The functional significance of recurrently mutated genes is then studied using primary human hematopoietic cells and mouse models.

The role of splicing gene mutations in MDS pathogenesis
Ongoing projects are focused on understanding the mechanism of MDS initiation and progression induced by mutations in genes that participate in pre-mRNA splicing identified by our group and others. Functional splicing assays, next-generation sequencing technology, and hematopoietic assays will be used to study primary human cells and mouse models harboring mutations.

The role of gene dosage in hematopoiesis
The laboratory is utilizing RNA interference (RNAi) in primary human and murine hematopoietic cells to study how gene dosage alters hematopoiesis. Knockout mice for specific MDS candidate genes are used to directly study the effects of haploinsufficiency on hematopoiesis.

All these studies involve state of the art technologies and incorporate functional genomics, bioinformatics, next-generation sequencing, stem cell and tumor biology, and mouse models of disease to study hematopoiesis.

Selected Publications:

