Regulating hematopoietic stem cell homeostasis and leukemogenesis

April 15 2008

In the April 15th issue of G&D, Dr. Richard Flavell (Yale University) and colleagues identify the c-Cbl protein as a critical repressor of hematopoietic stem cell (HSC) self-renewal. In addition to establishing a key role for protein ubiquitylation in HSC development, this finding posits c-Cbl as a potential target in research into stem cell engineering as well as cell-based leukemia treatments.

Dr. Flavell describes the work as elucidating “a novel dimension in our understanding the self-renewal of Hematopoietic stem cells."

Like all stem cell populations, HSC reply upon asymmetric cell division to generate two different daughter cells: one future stem cell, and another cell that will further differentiate into a more specialized cell type. Thus, a balance is struck between the production of new cell types and the renewal of the stem cell pool. However, imbalances between HSC self-renewal and differentiation can lead to hematologic malignancies like leukemia.

Dr. Flavell’s group discovered that the E3 ubiquitin ligase, c-Cbl, suppresses HSC self-renewal. The researchers generated transgenic mice deficient in c-Cbl, and demonstrated that these c-Cbl-mutant mice display an increased number of HSCs.

Lead author, Dr. Chozhavendan Rathinam, is confident that "our findings may facilitate the expansion and manipulation of hematopoietic stem cells for tissue engineering and stem cell based therapies."

Source: Cold Spring Harbor Laboratory