Docket #: S03-337

Progenitor profiling for preleukemia diagnosis, leukemia clinical staging, and prognosis of disease progression

Stanford researchers have identified methods to phenotype and stage leukemic conditions by differential analysis of the distribution of hematopoietic stem and progenitor cell subsets in clinical hematological samples. These methods represent a useful tool to diagnose preleukemia, prognose disease progression and monitor therapeutic success of the chosen cancer treatment. This disclosure also includes methods to identify leukemia stem cells, which are involved in disease progression and development of resistance to chemotherapeutic drugs. Unlike typical hematopoietic progenitor cells, leukemia stem cells have activated the beta-catenin pathway and, as a result, behave like hematopoietic stem cells, in that they acquire the capacity to self-renew and, thus, to facilitate the long-term proliferation of the cancer. The proliferation of leukemia stem cells can be blocked by inhibitors of the Wnt/beta-catenin pathway. This process can be monitored both in vitro using replating assays and in vivo using bioluminescent imaging of transplanted leukemia stem cell populations in a highly immunocompromised mouse model. It is critical to determine the efficacy of a chemotherapeutic agent or regimen in eliminating these self-renewing leukemia stem cells by monitoring the proliferation and self-renewal of leukemia stem cells. The technology described may have broader applications in the detection and elimination of cancer stem cells in other malignancies that have activated the Wnt/beta-catenin pathway such as colon, hepatocellular and breast cancer.

Applications

- Progenitor profiling can be used diagnostically to detect pre-leukemia as well as minimal residual disease
- Progenitor profiling allows clinical staging of leukemia

- Identification of leukemia stem cells via analysis of beta-catenin activation serves as a diagnostic tool to monitor and predict disease progression, relapse and development of drug resistance
- In vitro replating assays as well as in vivo engraftment studies via bioluminescent imaging of transplanted cells in a highly immunocompromised mouse model may be used as screening tools to detect factors and molecules that are active on cancer stem cells as well as normal hematopoietic stem cells
- Wnt/beta signaling pathway inhibitors can be used to inhibit leukemia stem cell self-renewal and proliferation but may be more broadly applicable in the elimination of other cancer stem cells

Advantages

- Diagnostic and prognostic information
- Rapid pre-clinical assessment of cancer stem cell phenotype
- Rapid pre-clinical in vitro and in vivo screening of response of cancer stem cell populations to specific molecularly targeted inhibitors
- Wnt/beta-catenin pathway inhibitors represent novel agents for cancer stem cell inhibition that are effective even in the setting of resistance to other molecularly targeted therapies

Publications

- US patent 7,816,088: Identification, isolation and elimination of cancer stem cells
- US patent 8,153,388: Methods for phenotyping of leukemias
- Jamieson CH, Ailles LE, Dylla SJ, Muijtjens M, Jones C, Zehnder JL, Gotlib J, Li K, Manz MG, Keating A, Sawyers CL, Weissman IL. Granulocyte-macrophage progenitors as candidate leukemic stem cells in blast-crisis CML. New England Journal of Medicine. 2004 Aug 12;351(7):657-67.

Patents

- Published Application: WO2005057172
- Published Application: 20080020407

- Published Application: 20110076683
- Issued: 8,153,388 (USA)

Innovators

- Catriona Jamieson
- Irving Weissman
- Laurie Ailles

Licensing Contact

Minxing Li

Licensing and Strategic Alliances Manager

Email