When Stem Cells Go Bad

By Robert L. Redner, MD

Stem cells. The very words bring a smile to the face of any hematologist. But in today's 2:00 p.m. Scientific Committee session on Stem Cells, Chair Craig T. Jordan, PhD, will introduce us to their dark side in the session on leukemic stem cells.

The notion of cancer stem cells derives from the finding that cancers contain heterogeneous populations of cells. In accordance with the well-known observation that many cancers temporarily remit but commonly relapse, the hypothesis has arisen that lurking within each cancer is a population of difficult-to-identify cancerous stem cells. Analogous to embryonic or hematopoietic stem cells, cancerous stem cells divide to give rise to two daughter cells, some of which regenerate the stem cell population with near-unlimited proliferation potential, and some of which differentiate to become more mature cancerous cells, which themselves may proliferate to give rise to the bulk of a tumor mass. The daughter cancer cell may be sensitive to chemotherapy, but the cancer stem cell, which hypothetically divides only rarely, is more resistant to chemotherapy — hence the ultimate futility of modern treatment strategies that fail to target the cancer stem cells. To truly cure cancer, one needs to exorcise the demons that are the cancer stem cells.

Scott Armstrong, MD, PhD, will lead off with a discussion of the unique immunophenotype that has been assigned to cells that can initiate leukemia in recipient mice. Leukemia-initiating cells, or leukemia stem cells (LSCs), are capable of generating progeny that are able to propagate the disease, as well as progeny that are more differentiated and incapable of transmitting leukemia. Dr. Armstrong will address the questions of whether acute myelogenous leukemia (AML) arises from mutation of normal stem cells, or whether more differentiated cells can be mutated to become LSCs. LSCs may indeed be very different from hematopoietic stem cells, raising hope that the LSCs may be targeted specifically.

Catriona Jamieson, MD, PhD, will continue the discussion by focusing on models of chronic myelogeneous leukemia (CML). Dr. Jamieson will present data indicating that blast crisis is typified by expansion of the granulocyte-macrophage progenitor pool (GMP). The ability of these cells to transplant leukemia into recipient mice suggests that the blast crisis GMP population is enriched for LSCs. The WNT signaling pathway is well known to be active in CML: the finding that these cells missplice a negative regulator of the Wnt/Beta catenin pathway, GSK3ß, may present a novel mechanism for enhancing LSC self-renewal.

Allison Blair, PhD, BSc, will discuss LSCs in acute lymphoblastic leukemia (ALL). For years, the different acute ALL subtypes have been considered to represent clonal expansion of lymphoid cells that had been transformed at different maturation stages. Dr. Blair's data challenge this long-held hypothesis. Dr. Blair will discuss new experimental data that indicate that some subtypes of childhood ALL may have a more primitive cell of origin than previously thought.

An encore presentation is scheduled for tomorrow morning at 9:30 a.m. And those drawn to the dark side will not want to miss Tuesday's Presidential Symposium on Cancer Stem Cells. Bring your light sabers!