How long do stem cells live?

March 1 2011

When patients receive a bone marrow transplant, they are getting a new population of hematopoietic stem cells. Fresh stem cells are needed when a patient is low on red blood cells, as in anemia, or white blood cells, which can be caused by cancer or even cancer treatments such as irradiation or chemotherapy. The problem is that a bone marrow transplant might not succeed because the transplanted stem cells don't live long enough or because they proliferate too well, leading to leukemia.

To help determine how long a bone marrow (stem cell) graft will last, researchers at Sanford-Burnham Medical Research Institute (Sanford-Burnham) have developed a mathematical model that predicts how long a stem cell will live and tested those predictions in a mouse model. The study, led by Christa Muller-Sieburg, Dr. rer. nat., was published online the week of February 28, in the journal Proceedings of the National Academy of Sciences.

"It has long been assumed that stem cells are immortal – they continue to self-renew, thus generating more stem cells that collectively can outlast an individual's life," said Dr. Muller-Sieburg, professor in Sanford-Burnham's Stem Cells and Regenerative Biology Program. "But now we have found that each stem cell is pre-programmed to self-renew only for a set amount of time that, in mice, ranges from a few months to several years. So we created a computer program that predicts that lifespan."

Researchers drew blood from transplant recipients, took a few initial measurements of the mature white blood cells generated from the

transplant, and entered those parameters into a computer program that predicts their lifespan. This information was then compared to the stem cells' true lifespan. Some stem cells lasted five months and others more than three years, but again and again the computer program predicted survival time with surprising accuracy.

Dr. Muller-Sieburg and her colleagues found that stem cell self-renewal is strictly regulated to successfully negotiate a precarious balance: too much self-renewal results in leukemia, while too little leads to bone marrow failure. This new understanding now allows them to better predict the conditions that lead to normal stem cell proliferation.

Not only are these findings relevant to bone marrow transplants, they could also have implications for regenerative medicine. The safety and efficacy of using embryonic and other stem cells for tissue regeneration will depend on harnessing and precisely controlling their proliferative capacity. By providing a better understanding of how stem cells proliferate, and when they die, this lifespan prediction program could help improve their therapeutic potential for diabetes, Alzheimer's disease and other conditions.

Mathematical modeling has other benefits, too. According to lead author Hans Sieburg, Dr. rer. nat, "Computer simulation allows us to generate a hypothesis, make predictions about what should be true, and then better plan our experiments in a way that requires fewer animal experiments."

More information: Sieburg HB, Rezner BD, Muller-Sieburg CE. Predicting clonal self-renewal and extinction of hematopoietic stem cells. *Proceedings of the National Academy of Sciences*. February 28, 2011.

Provided by Sanford-Burnham Medical Research Institute