Hormone reduces risk of heart failure from chemotherapy

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Recent studies have shown that the heart contains cardiac stem cells that can contribute to regeneration and healing during disease and aging. However, little is known about the molecules and pathways that regulate these cells. Now, a new study utilizing a heart failure model is providing insight into one way to coax the cardiac stem cells into repairing the damaged heart. The research, published by Cell Press in the August 2011 issue of the journal *Cell Stem Cell,* finds that low doses of erythropoietin (EPO), a hormone best known for controlling the production of red blood cells, might reduce the risk of heart failure associated with some anticancer therapies.

Chemotherapy with doxorubicin (DOX) has been used effectively to treat a broad range of cancers but is limited because of severe side effects, most notably heart failure. Likewise, blocking STAT3, an important factor that drives tumor growth has been associated with heart failure. To learn more about the activity of cardiac stem cells under these conditions, senior study author, Dr. Denise Hilfiker-Kleiner from the Medical School Hannover in Germany, and colleagues studied cardiac stem cells in mice that were lacking the STAT3 gene in their hearts or were treated with DOX.

Dr. Hilfiker-Kleiner and colleagues observed that in both groups of mice, cardiac stem cells displayed an impaired ability to form new blood vessels which are essential for oxygen delivery to the heart muscle. Both sets of mice produced less EPO in their heart muscle than untreated controls. The researchers went on to demonstrate that EPO binds to

cardiac stem cells and is required to maintain the signaling molecules necessary for production of new blood vessels. Importantly, when the mice were given a synthetic EPO derivative at a low dose which did not affect red blood cell production, stem cell differentiation to blood vessel cells was restored and cardiac function was preserved. "Short-term EPO administration at low doses seems an attractive avenue to pursue for protecting the heart during chemotherapy and might have broader applications in cardiac regeneration," concludes Dr. Hilfiker-Kleiner.

Provided by Cell Press