New strategy improves stem cell recruitment, heart function and survival after heart injury

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A new study in mice shows that a dual therapy can lead to generation of new blood vessels and improved cardiac function following a heart attack. The research, published by Cell Press in the April 3rd issue of the journal *Cell Stem Cell*, provides an explanation for the ineffectiveness of current stem-cell-mobilizing therapies and may drive design of future regenerative therapies for the heart.

Stem-cell-based therapies are an attractive option for the treatment of heart damage after a heart attack, also known as myocardial infarction (MI). However, although animal studies using stem cells derived from the bone marrow have elicited some improvement in cardiac function, human trials have not been as successful. "Modern approaches have to focus on the process of cardiac homing to improve the clinical outcome of stem cell therapies," explains senior study author, Dr. Wolfgang-Michael Franz from Ludwig-Maximilians University.

The stromal-cell-derived factor, type I (SDF-1) is the main chemical that guides stem cells to home in on damaged heart tissue. Because SDF-1 is inactivated by CD26/dipeptidylpeptidase IV (DPP-IV), endogenous stem cell localization to the heart is not optimal. The researchers used genetic or pharmacologic inhibitors of CD26/DPP-IV to slow degradation of SDF-1 in mice with surgically induced MI. They also treated the mice with granulocyte colony stimulating factor (GCSF), a commonly used drug that mobilizes multiple stem cell populations from the bone marrow to the blood.

The researchers found that genetic or pharmacologic inhibition of CD26/DPP-IV combined with G-CSF treatment decreased DPP-IV and stabilized activated SDF-1 in the heart, thereby enhancing the recruitment of circulating blood forming precursor cells, or EPCs (endothelial progenitors) to this organ. Further, the combined treatment increased formation of new blood vessels and improved both survival and cardiac function after MI.

The results represent the first experimental evidence that inhibition of DPP-IV combined with G-CSF enhances cardiovascular regeneration. "Our findings may contribute essential new aspects for design of future stem cell trials, since the key issue of all therapeutic stem cell approaches emerges to be the process of cardiac homing," says Dr. Franz. "We propose the use of combined DPP-IV inhibition and G-CSF application as a new therapeutic concept for future stem cell trials."

Source: Cell Press (news : web)