

# Promising and perilous? The ambivalent role of the CXCL12/ CXCR4 axis in heart repair

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The chemokine CXCL12 acts as a chemical signal which mobilizes hematopoietic and other types of stem cells to leave the bone marrow and enter the circulation. Secretion of CXCL12 also guides these cells to sites at which the perfusion of tissue is sub-optimal due to localized obstruction of blood flow. These capabilities have made CXCL12 and its cognate receptor CXCR4 interesting candidates for therapies aimed at mitigating the effects of damage to the heart caused by myocardial infarction.

A team of researchers led by Professor Christian Weber of the Medical Center of the University of Munich has now taken a closer look at the normal physiological function of this ligand-receptor couple. Their results reveal that the molecules have "rather ambivalent roles," as Weber puts it.

[Myocardial infarction](#) remains one of the leading causes of death in Western societies. The condition occurs when parts of the heart muscle can no longer be adequately supplied with oxygen because blood flow through the coronary arteries is impeded. Researchers have therefore suggested that CXCL12 and CXCR4 could perhaps be used therapeutically to direct stem cells required for the formation of new blood vessels to migrate into ischemic, i.e. poorly perfused, tissues and thus help to increase blood flow in such areas.

"The precise [physiological functions](#) of the chemokine and its receptor are poorly understood, although these are the crucial determinants of

their therapeutic potential and of possible side-effects," Weber points out. "We therefore studied the effects of infarction in an animal model in which the amount of CXCR4 produced is specifically reduced. We focused on the molecular and cellular consequences of infarction, particularly with respect to the recovery of [cardiac function](#), formation of [scar tissue](#), severity of inflammation, and neovascularization of [heart muscle](#)."

To their surprise the researchers found that reduction of the CXCR4 level correlated with significant reductions in infarct size and the degree of tissue inflammation, but that recovery of blood flow and neovascularization were concomitantly decreased. These opposing effects together meant that heart function was equally impaired whether or not the level of CXCR4 function was reduced.

"However, we did see some evidence for an improvement in adaptation to sub-optimal levels of oxygen," Weber remarks. "Although we cannot assume that these results are immediately applicable to the human heart, they do point toward the possibility – especially in the case of systemic therapy – of quite critical side-effects. We should perhaps focus on more localized approaches, such as the direct injection of stem cells with higher levels of CXCR4, or of CXCL12 variants that remain confined to the damaged areas of the heart or retain their activity in the coronary arteries for longer." (suwe/PH)

**More information:** Double-Edged Role of the CXCL12/CXCR4 Axis in Experimental Myocardial Infarction, Elisa A. Liehn et al.

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