Monocyte migrations

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LMU researchers led by Christian Weber have, for the first time, elucidated how cells that promote the development of atherosclerosis find their way to the blood vessel wall, where they stimulate the formation of obstructive deposits.

Atherosclerosis is one of the commonest causes of death in modern societies. The condition is characterized by the build-up of fatty deposits called atherosclerotic plaques on the inner surfaces of arteries, which restrict, and may eventually cut off, blood flow. The deposits can also be dislodged from their site of origin and may then block major vessels in the heart or the brain, leading to life-threatening myocardial infarction or stroke.

Monocytes, an important class of white blood cells, are known to contribute significantly to the development of atherosclerosis. They are actively recruited to atherosclerotic lesions, and promote plaque development by sustaining a chronic inflammatory reaction.

Inhibition of monocyte recruitment therefore offers a way of interrupting the build-up of plaques. However, one first needs to know how the monocytes are actually localized to the vessel wall. Professor Christian Weber and Dr. Maik Drechsler of the Institute for Prophylaxis and Epidemiology of Cardiovascular Disease at LMU, in collaboration with Oliver Söhnlein of LMU and a team at the Academic Medical Center in Amsterdam, have now shown that the receptor molecules CCR1 and CCR5 are crucially involved in the process by which monocytes are recruited to the vessel wall. This process is made up of a

sequence of distinct steps, including adhesion of the endothelial cells that form the arterial wall, and their subsequent transmigration into the bloodstream by infiltration between neighboring endothelial cells, following activation of the receptors by binding of their respective ligands.

The new findings correct a commonly held view of the precise function of the CCR2 receptor in the recruitment of monocytes. "In contrast to what has been assumed so far, this receptor does not mediate the infiltration of monocytes into the vessel wall; instead, like another chemokine receptor, CXCR2, it controls their mobilization from the bone marrow into the bloodstream," says Oliver Söhnlein.

The receptor molecules CCR1 and CCR5 therefore present promising targets for the development of novel approaches to the treatment of atherosclerosis, using agents that inhibit their interaction with their respective binding partners, either directly or indirectly.

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