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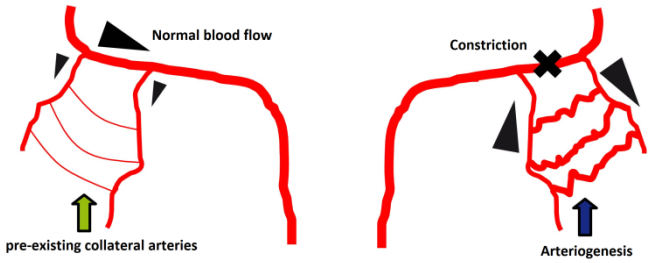
STIMULATION OF ARTERIOGENESIS FOR THE PREVENTION OF MYOCARDIAL INFARCTION

CHALLENGE

Arteriogenesis is a physiological process characterised by an increase in the diameter of existing arterial vessels. It is induced by shear force on the vessel wall upon increased blood flow through the vessel. Narrowing of main arteries (stenosis) due to e.g. atherosclerosis intensifies the blood flow through smaller collateral arteries. As a consequence, arteriogenesis leads to remodelling of these collateral arteries into functional arteries with improved blood flow and creates a biological bypass. Thus, stimulation of this process may offer novel treatment options for patients being at risk for the development of myocardial infarction.



Induction of arteriogenesis upon stenosis

TECHNOLOGY DESCRIPTION

Many details of how exactly mechanical shear stress is translated into the outgrowth of existing collateral arteries are still unknown. In arteriogenesis these mechanistic aspects are linked to the activation of inflammatory processes with bradykinin receptor B1 (B1R) signaling being a crucial component. In particular it could be demonstrated that B1R signaling on monocytes is of major importance. These circulating leukocytes are a key factor in remodeling collateral arterial tissue, and in-vitro experiments show that treatment of monocytes with a B1R agonist strongly increases their migration.

B1R knock-out mice showed a pronounced reduction in collateral arterial growth after vessel occlusion. Also, these animals possessed fewer leukocytes. Infusion of leukocytes from WT mice could restore the arteriogenic capacity. Blocking of B1R signaling with known B1R antagonists in WT mice showed similar reductions like in knock-out animals. Finally, in a rat model for cerebral arteriogenesis treatment with a specific B1R agonist showed a significant increase in collateral artery diameter compared to control animals. The offered technology provides a broad range of B1R agonists for the stimulation of arteriogenesis. Patents protecting the use of such B1R agonists as medication for patients at risk of myocardial infarction have been granted in the US and in Europe.

COMMERCIAL OPPORTUNITY

Available for licensing or collaboration

PATENT SITUATION

US2013/0136717 (granted 2016) and EP2568995 (granted 2016) with priority from May 14, 2010

FURTHER READING

Hillmeister et.al., Arteriogenesis is modulated by bradykinin receptor signaling, Circ. Res. 2011, 109(5), 524-33.

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