Animal Model

Kinin B1 Receptor Knock-Out Mice

Reference Number 03-00145

Abstract

Challenge

Kinins are important mediators in cardiovascular homeostasis, inflammation, and nociception. After ischemic injury, enhanced kinin generation may contribute in processes responsible for tissue healing. By exploiting the gene knockout strategy, our scientists demonstrated that the endogenous B1 signalling is indeed essential for developing new blood vessels. Seminal studies from our scientists showed that B1 pharmacological blockade inhibits capillary proliferation in response to limb ischemia. Moreover, they showed that B1 antagonism severely impairs blood perfusion recovery of ischemic muscles. Another major novelty is the observation that genetic disruption of the B1 results in the absolute failure to mount reparative angiogenesis. B1 stimulation by local administration of a specific receptor agonist has a potential in therapeutic angiogenesis. In vitro studies showed that engagement of kinin B1 by des-Arg10-kallidin or R916 stimulates proliferation of coronary endothelial cells.

Technology

Ligands activating the B1 receptor possess a significant therapeutic potential for the treatment of peripheral ischemia. Administration of B1 agonists could be safer than adenovirus-mediated growth factor gene delivery that reportedly produces harmful side effects mainly attributed to viral vectors. Receptor agonist are devoid of immunogenic activity. B1 receptor antagonists might be envisaged as therapeutic reagents to combat the pathological angiogenesis in cancer and chronic inflammatory diseases. Thus, B1 pharmacological manipulation might open new avenues for the treatment of a wide range of diseases characterized by impaired or excessive vascular growth.

Commercial Opportunity

A Kinin B1 Receptor Knock-Out Mouse was developed, where breeding pairs are available. Using this animal model it is possible to analyse the mechanisms of reparative angiogenesis as well as to evaluate therapeutic strategies against diseases coming along with pathological angiogenesis like cancer and inflammatory diseases and with ischemic injuries like coronary heart disease and stroke.

Further Reading

- Emanueli et al., Circulation, 2002, Jan 22;105(3):360-6
- Pesquero et al., PNAS, 2000, Jul 5, 97(14): 8140-8145

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