Selective inhibition of vascular smooth muscle cells to improve safety and efficacy of anti-restenotic therapy

Technology #cu12261

Coronary artery disease (CAD) is a leading cause of death in the US and throughout the world. While balloon angioplasty and/or stent implantation is a common surgical treatment, the occurrence of restenosis in these patients leads to future complications and additional surgical intervention. To this end, therapies that utilize drug-eluting stents (DES) non-selectively reduce vascular smooth muscle cell (VSMC) growth, minimizing restenosis, but also inhibit growth of vascular endothelial cells (VEC), leading to post-operative thrombosis and death. This technology describes a microRNA-based (miRNA-based) approach to prevent restenosis by inhibiting proliferative VSMCs, while selectively promoting reendothelialization and persevering VEC function. As such, this technology retains the patency maintenance required of CAD treatments while lowering the risk of post-operative thromboses, ultimately improving long-term patient outcomes.

Simple hybrid vector to enable a safer and efficacious anti-restenotic therapy

This technology describes the creation of a vector that aims to reduce restenosis associated with treatment of CAD while decreasing risk of post-operative complications. While drugs currently approved to coat stents can effectively limit restenosis by activating the cell cycle inhibitor p27, they don’t discriminate between proliferating VSMCs and ECs. Consequently, it delays reendothelialization and vascular healing, thus increasing the risk of late thrombosis following angioplasty. By incorporating the target sequences for the VEC-specific mRNA, miR-126, into the p27 expressing vector, this technology is able to selectively express p27 where appropriate. As a result, this approach would selectively inhibit vascular smooth muscle cell proliferation, and thus restenosis, with minimal impact to the growth of VECs.

A prototype of the technology has been tested in vivo and been shown to selectively inhibit the growth of VSMCs while preserving the function of VECs.

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Applications:

• Inhibition of VSMC proliferation in other contexts, such as atherosclerosis, arterial injury and vascular access failure in hemodialysis patients
• Depletion of mixed cultures of VSMC in laboratory experimentation
• A model of defective growth in VSMC
• Selective inhibition of growth of any number of cell types

Advantages:

• Reduce restenosis associated with surgical interventions for coronary artery disease
• Lowers the risk of post-operative thrombosis associated with drug eluting stents
• Can achieve restenosis reduction and minimize post-operative complications in a single comprehensive treatment
• Simple process to incorporate the miRNA into the p27 vector

Patent Information:

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Related Publications:


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