

YY1 Gene Therapy for the Prevention of Vascular Restenosis

Business Opportunity

An opportunity exists for a medical device or biotechnology company to work with the University of New South Wales (UNSW) to develop Yin Yang 1 (YY1) for the prevention of vascular occlusion in several applications.

The Problem

Over 6 million surgical and/or interventional procedures aimed at restoring blood flow are performed annually. These include balloon angioplasty, stenting, vein bypass graft and haemodialysis access graft.

Graft failure after bypass surgery is caused by aggressive growth of a special type of cells called vascular smooth muscle cells. These cells thicken the vessel wall (or intimal hyperplasia) and cause occlusion (or stenosis).

- Restenosis in balloon angioplasty occurs within 6 months in up to 40% of patients.
- Graft occlusion in by-pass surgery occurs in up to 20% of patients within 12 month.
- Access graft failure occurs in over 50% of in haemodialysis patients within 1 year of insertion.

Bypass graft failure, access graft stenosis and restenosis are principal causes of morbidity and hospital stays, costing billions of dollars in the US alone.

Poor long-term potency and the lack of suitable pharmacologic therapies provide a compelling need for the development of new strategies to block this process.

YY1 Anti-Restitotic Properties

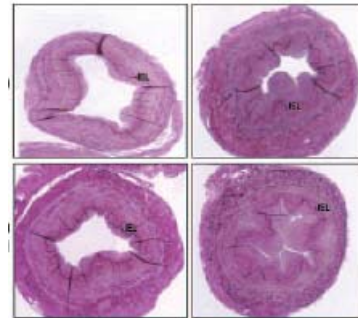
Yin Yang 1 (YY1) is a GLI-Kruppel-type zinc finger nuclear protein transcription factor that is expressed during vascular injury, such as following access graft insertion.

Researchers at UNSW have found that forced expression of YY1 inhibits smooth muscle cell proliferation and neointimal formation in human, rat and rabbit blood vessels, but does not inhibit vascular endothelial cell proliferation.

Technical Development

Researchers have constructed and validated adenoviral, retroviral and plasmid YY1 vectors generating exogenous YY1 protein.

Excellent YY1-specific antibodies are available (these are used in Western blotting, immunoprecipitation, immunocytochemistry, immunohistochemistry).



Ex-vivo transduction of human saphenous veins with adenoviral YY1 expression vector (Ad-YY1). Top Left: Representative cross section of human saphenous vein explants. Top Right: vascular wall thickening at 14 days following serum exposure, showing thickening of the internal elastic lamina. Bottom Left: ex-vivo transduction of human saphenous veins with Ad-YY1 reduces vascular wall thickening. Bottom Right: ex-vivo transduction of human saphenous veins with adenoviral LacZ does not prevent vascular wall thickening.

Commercial Applications

Yin Yang 1 (YY1) potentially provides an alternative or adjunct to treatment for restenosis. Applications and delivery mechanisms for this technology include:

- Vascular stent – drug eluting stents, coated metal stents, biodegradable stents.
- Balloon angioplasty- capillary injection.
- Coronary artery by-pass graft (CABG) occlusion – via ex vivo transduction, branching stent or via impregnation in a polymer vascular wrap.
- Peripheral by-pass surgery – coated synthetic stent-grafts.
- Haemodialysis access graft stenosis – coated synthetic access graft with drug-eluting collar or vascular wrap.

Patent Protection

Patent application is pending in Australia, Europe and the US.

Investment Opportunity

NSi seeks to partner with a medical device or biotechnology company to develop a stent or vascular wrap capable of delivering YY1, a novel anti-restitotic biologic.

The Scientific Team

Professor Levon Khachigian and his team at the Centre for Vascular Research at UNSW have an exceptional track record in research and commercialisation, with over 130 publications and numerous patents.

Further Information:

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