

# Licensing Opportunity



## Biomarkers for restenosis risk assessment

- Unique markers to assess the risk for stent restenosis
- Clinically validated SNPs

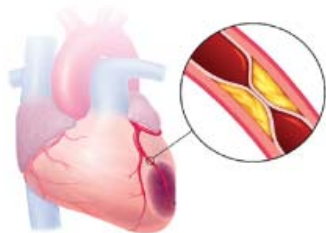
Cardiovascular diseases

2011

## Background

Atherosclerotic lesions in coronary arteries that obstruct normal blood flow are the cause of myocardial infarction. The intervention cardiologist restores the arterial lumen by intravascular balloon-angioplasty and subsequent placement of a stent. Re-occlusion of the stented artery, denoted as in-stent restenosis, is a serious clinical problem after stent placement. Drug-eluting stents (DES) effectively prevent in-stent restenosis, but are associated with an increased risk for in-stent thrombosis.

The intervention cardiologist needs to decide whether to use a bare-metal stent (BMS) or a drug eluting stent DES. To avoid overtreatment of patients we need to predict a patient's risk to develop in-stent restenosis before treatment. Currently the criteria upon which cardiologists base their decision are risk factors such as diabetes, LDL-cholesterol levels as well as location and length of the lesion. We propose that assessment of the risk of individual patients to develop in-stent restenosis will significantly contribute to personalized intervention.

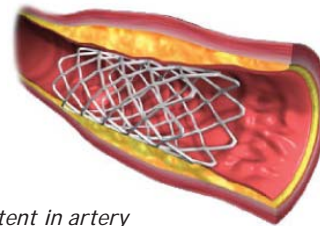


*Heart with atherosclerotic lesion in the coronary artery*

## The Technology

AMC scientists have identified single nucleotide polymorphisms (SNP) that associate with the risk to develop restenosis in response to balloon angioplasty. When incorporated in a SNP detection kit, these SNPs may be used to diagnose a patient with increased risk to develop restenosis before performing coronary angioplasty.

This will provide intervention cardiologists with a strong decision criterion to choose between treatment with a BMS or with a DES and thus avoid under-treatment as well as over-treatment of individual patients.



*Stent in artery*

## Applications

Diagnostic tests to:

- diagnose the risk of individual patients to develop restenosis before performing coronary angioplasty interventions.
- identify patients at risk for other smooth muscle cell proliferative vascular diseases such as vein-graft disease, arteriovenous shunt malfunctioning and (in-stent) restenosis in peripheral arteries.

## R&D Status

A single p27Kip1 SNP and a haplotype composed of three Nurr1 SNPs predict the risk of an individual to develop in-stent restenosis with high sensitivity and specificity.

The p27Kip1 SNP identifies patients with a 1.7 to 3.6 fold higher risk to develop in-stent restenosis. (In two different populations hazard ratios were found of 0.28; 95% confidence interval, 0.10-0.77 and 0.61; 95% confidence interval, 0.40-0.93, respectively).

The comprehensive Nurr1 haplotypes allow identification of individuals with a 1.6 to 3.1 fold increased risk to develop restenosis.

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## Intellectual Property

Priority date: May 2009. PCT filed in May 2010

## Inventors

Prof. dr. Carlie J.M. de Vries and prof. dr Robbert J. de Winter. Carlie de Vries is a molecular cell biologist with a strong background in vascular cell biology and atherosclerosis. She is heading a research group at the Academic Medical Center in Amsterdam. Robbert de Winter is an intervention cardiologist at the same Institute with an extensive track record in research and execution of multicenter clinical trials in interventional cardiology.

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## Key publications

1. van Tiel CM, Bonta PI, Rittersma SZ, Beijk MA, Bradley EJ, Klous AM, Koch KT, Baas F, Jukema JW, Pons D, Sampietro ML, Pannekoek H, de Winter RJ, de Vries CJ. p27kip1-838C>A single nucleotide polymorphism is associated with restenosis risk after coronary stenting and modulates p27kip1 promoter activity. *Circulation*. 2009;120(8):669-76.
2. Bonta PI, Pols TW, van Tiel CM, Vos M, Arkenbout EK, Rohlena J, Koch KT, de Maat MP, Tanck MW, de Winter RJ, Pannekoek H, Biessen EA, Bot I, de Vries CJ. Nuclear receptor Nurr1 is expressed in and is associated with human restenosis and inhibits vascular lesion formation in mice involving inhibition of smooth muscle cell proliferation and inflammation. *Circulation*. 2010;121(18):2023-32.