Non-invasive ultrasound-based cardiovascular imaging in mouse models of atherosclerosis

AKADEMISK AVHANDLING

som för avläggning av medicine doktorsexamen vid Göteborgs Universitet kommer att offentligen försvaras i föreläsningssalen Arvid Carlsson, Academicum, Medicinaregatan 3, Göteborg, fredagen den 15 februari 2008 klockan 9.00

av

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Avhandlingen baseras på följande fem delarbeten:

Proximal to middle left coronary artery flow velocity ratio, as assessed using color Doppler echocardiography, predicts coronary artery atherosclerosis in mice.

II. **Wikström J, Grönros J, Bergström G, Gan LM**
Functional and morphologic imaging of coronary atherosclerosis in living mice using high-resolution color Doppler echocardiography and ultrasound biomicroscopy.

Non-invasive real-time imaging of atherosclerosis in mice using ultrasound biomicroscopy.
*Atherosclerosis.* 2007 Feb;190(2):313-20. Epub 2006 May

IV. **Grönros J, Wikström J, Berke Z, Andreasson AC, Lundin S, Gan LM**
High circulatory interleukin-18 levels are associated with advanced coronary artery atherosclerosis in mice
*Submitted*

V. **Grönros J, Wikström J, Brandt-Eliasson U, Forsberg GB, Behrendt M, Hansson GI, Gan LM**
Effects of rosvastatin on cardiovascular morphology and function in an ApoE knockout mouse model of atherosclerosis.
*Submitted*
Non-invasive ultrasound-based cardiovascular imaging in mouse models of atherosclerosis

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ABSTRACT

Atherosclerosis is a chronic multi-factorial vascular disease. It generally requires large clinical settings and over many years to study the disease progression in man. Genetically modified mouse models of atherosclerosis have dramatically increased research feasibility within this area. However, for optimal translational studies, it is increasingly important to explore how human-like these atherosclerotic mouse models demonstrate their disease phenotype and respond to established cardiovascular interventions.

The aims of this thesis were to develop and apply in vivo translational techniques to study living atherosclerotic mice, with human-relevant disease phenotype.

Color Doppler guided echocardiography and a high-frequency ultrasound biomicroscope were used for imaging of peripheral and coronary artery function and morphology. The potential role of IL-18 in mice was explored in relationship to mouse coronary artery disease. Finally temporal effects of rosvastatin on cardiovascular phenotype were studied in an ApoE knockout mouse model of atherosclerosis.

This thesis illustrates that it is possible to investigate both central and peripheral atherosclerosis in living mice using ultrasound-based techniques. Our findings may also suggest an important role of IL-18 in late stage atherosclerosis in an advanced model of atherosclerosis. Finally, this particular ApoE knockout mouse model showed time-dependent beneficial cardiovascular effects following rosvastatin treatment.

The established translational functional and morphological imaging platform in combination with our human-like statin-responding mouse model, provide us with powerful tools for future atherosclerosis research.

Keywords: atherosclerosis, ultrasound-based imaging, cardiovascular disease, coronary artery, mouse, color Doppler echocardiography, ultrasound biomicroscopy, statin