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

Julia Grönros
Fil. Mag.

Fackultetsopponent:
Docent John Pernow, MD PhD
Enheten för Kardiologi
Karolinska Institutet
Solna, Sverige

Avhandlingen baseras på följande fem delarbeten:

I. **Grönros J, Wikström J, Hägg U, Wandt B, Gan LM**
Proximal to middle left coronary artery flow velocity ratio, as assessed using color Doppler echocardiography, predicts coronary artery atherosclerosis in mice.
Arterioscler Thromb Vasc Biol. 2006 May;26(5):1126-31. Epub 2006 Mar 2.

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.
J Am Coll Cardiol. 2005 Aug 16;46(4):720-7.

III. **Gan LM, Grönros J, Hägg U, Wikström J, Theodoropoulos C, Friberg P, Fritsche-Danielsson R**
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 rosuvastatin on cardiovascular morphology and function in an ApoE knockout mouse model of atherosclerosis.
Submitted

The Sahlgrenska Academy
AT GÖTEBORG UNIVERSITY
Institute of Neuroscience and Physiology

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

Julia Grönros, 2008, Department of Physiology, Institute of Neuroscience and Physiology, Sahlgrenska Academy, Göteborg University, Box 432, 405 30 Göteborg, Sweden

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 rosuvastatin 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 rosuvastatin 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

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