Göteborg, 2016

The pro-atherogenic role of intimal hyperplasia

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Blå stråket 5, Göteborg, den 2017-01-25, klockan 09.00

av Siavash Kijani

Fakultetsopponent:
Professor Katariina Öörni
Wihuri Research Institute, Biomedicum, Helsinki, Finland

Avhandlingen baseras på följande delarbeten

I. Intimal hyperplasia induced by vascular intervention causes lipoprotein retention and accelerated atherosclerosis in mice

Siavash Kijani, Ana Maria Vázquez, Malin Levin, Jan Borén and Per Fogelstrand

Submitted

II. Non-toxic cadmium accelerates subendothelial retention of atherogenic lipoproteins in humanized atherosclerosis–susceptible mice

Siavash Kijani, Göran Bergström, Malin Levin, Lars Barregård, Björn Fagerberg, Per Fogelstrand and Jan Borén.

Manuscript

III. Filter-Dense Multicolor Microscopy

Siavash Kijani, Ulf Yrlid, Maria Heyden, Malin Levin, Jan Borén, Per Fogelstrand.

PLoS ONE, March 2015

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN

GÖTEBORGS UNIVERSITET

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The pro-atherogenic role of intimal hyperplasia

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Atherosclerosis is a leading cause of mortality worldwide, and results from accumulation of plasma lipoproteins, mainly low-density lipoproteins (LDL), in the sub-endothelial layer of the arterial wall. In this thesis, I investigated how structural changes of the vessel wall can make the vessel more prone to developing atherosclerotic lesions.

Project 1: Accelerated atherosclerosis occurs following vascular interventions, such as percutaneous coronary intervention and implantation of saphenous vein grafts. However, the cause of the accelerated atherogenesis is not known. We found that intimal hyperplasia induced by vascular interventions makes the vessel wall highly susceptible to LDL retention and accelerated atherosclerosis by a mechanism that can be targeted by glycosaminoglycan (GAG)-binding antibodies.

Project 2: Cadmium is an important risk factor for athero-sclerosis, but the underlying mechanism for how cadmium increases the risk of atherosclerosis is unclear. We observed: (1) increased expression of perlecan and the GAG-chain modifying enzyme CHST3 in arteries following local exposure to cadmium; and (2) increased LDL-binding in proteoglycans isolated from cells cocultured with cadmium. Finally, we showed that local cadmium exposure increased LDL retention in the arterial wall.

Project 3: Immunofluorescence microscopy is a method used to study the spatial location of proteins in tissues and cells. Here we present an enhanced multi-fluorescence setup based on condensed filter sets that are more specific for each fluorochrome and allow for a more efficient use of the light spectrum.

Keywords: Atherosclerosis, Vascular intervention, Multicolor microscopy, Cadmium, Intimal hyperplasia

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