Novel markers and mechanisms of plaque rupture governed by smooth muscle cells

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I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

X I do not have any potential conflict of interest
Clinical Problem: Tools lacking for early diagnosis of unstable carotid atherosclerosis

- Needed: Integrative risk profiling to stratify 1) patients and 2) stable and unstable plaques

- Patient-centered molecular analyses can lead to improved tools for diagnosis and treatment of unstable atherosclerosis
**Translational research platform:**
**Biobank of Karolinska Endarterectomies**

- Unique, multidisciplinary platform founded in 2003 (1500 patients)
- Established, world’s largest resource of plaque transcriptomic & proteomic data
- **OPEN** for collaborations !!!

- **Phase I:** Clinical Analyses & Discovery
- **Phase II:** Exploration
- **Phase III:** Translation

➤ **Rationale:** Entry into the studies directly from human disease

- Workshop on biobanking by Maegdefessel L, Friday 11:30, Pavillon
Hypothesis:

The full knowledge of key expression signatures can help us derive a definition of various SMC phenotypes that coexist in the vessel wall, and provide targets for prevention or therapy.
Using an integrative approach, we identified PDLIM7 and a panel of genes that reflect the altered phenotype of SMCs in vascular disease and could be early sensitive markers of SMC dedifferentiation.
Combined plaque evaluation by US and microarrays reveals BCLAF1 as a novel regulator of SMC transdifferentiation in atherosclerosis

- SMC transdifferentiation is associated with plaque echolucency and BCLAF1 regulates SMC survival by transition into a macrophage-like phenotype

Rykaczewska U et al, in submission to Circ Res
PCSK6 is a key protease in the control of SMC function in vascular remodeling

- PCSK6 is enriched in vascular remodeling, and functionally linked with SMC modulation in response to inflammation, mechanistically via activation of MMP14

Perisic L et al, Arterioscl Thromb Vasc Biol 2013
Perisic Matic L et al, in revision for Circ Res 2017
Macro-calcification in advanced plaques correlates with altered SMC phenotype and ECM composition, and repressed inflammation.
**Summary:**

**Novel markers of SMCs in plaques**

- PDLIM7
- PCSK6
- BCLAF1
- PRG4

**Significance:**

These markers are key drivers of SMC-related processes in human plaques and thus promising targets for exploration in diagnostic and therapeutic approaches.
Collaborators
National/International

Vascular Surgery
Clinic/Research Lab

Group Leader: Prof Ulf Hedin

PIs: Joy Roy, Rebecka Hultgren, Ljubica Matic, Anton Razuvaev

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Research Nurse: Olga Nilsson

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Research coordinator: Siw Frebelius

KI/Sweden

CMM: Per Eriksson, Lars Maegdefessel, Daniel Ketelhuth, Ewa Ehrenborg, Göran Hansson,
SciLife: Jacob Odeberg, Janne Lehtiö

ICMC: Bo Angelin

KTH: Christian Gasser,
Neuroradiology:
Staffan Holmin

Huddinge: Peter Stenvinkel

Stanford: Nick Leeper, Tom Quertermous

CARIM: Leon Schurgers

LUMC: Jan Lindeman

King’s: Manuel Mayr

Canada: Robert Day, Katey Reyner, Ruth McPearson

Boston: Kathryn Moore

Germany: Stephanie Dimmeler, Reinier Boon, Kostas Stellos

BiKE statistics
- >70 papers published since 2004
- >70 active projects
- 15 PhD theses