Why do men and women differ in atherosclerotic cardiovascular disease?

- What we have learnt from proteomics

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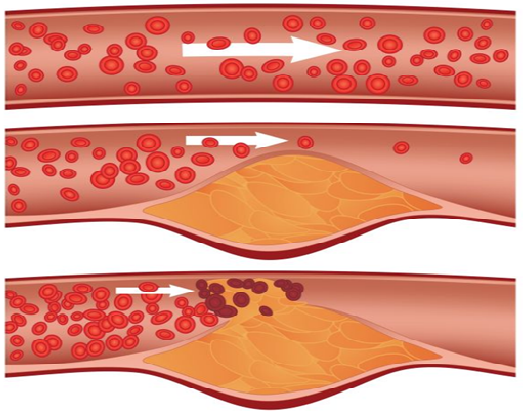
Agenda

- Atherosclerosis
- Proteomic approaches
- ACVD proteomics & sex differences
- Future – our work
- Other applications

"*New* analytical methods"

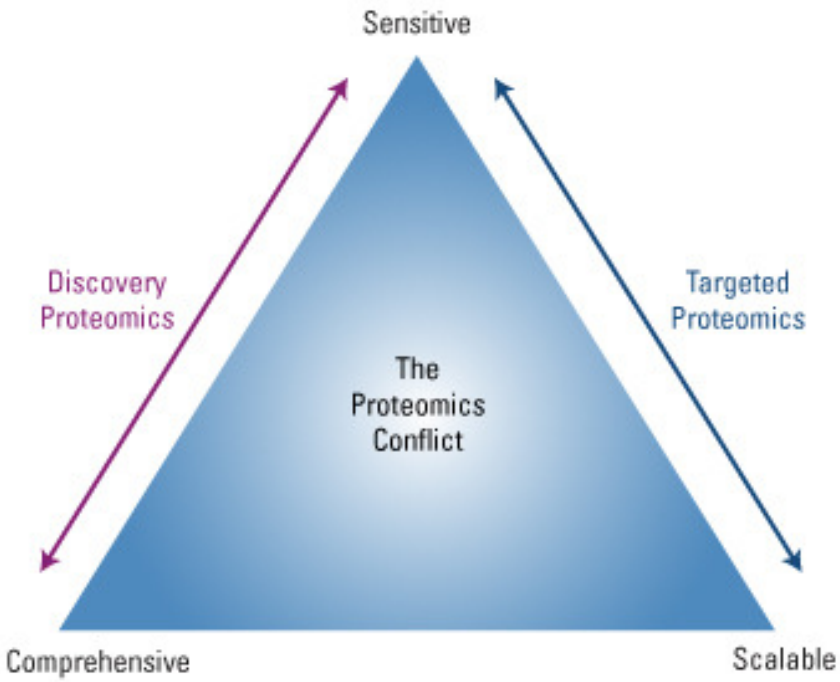
Atherosclerosis

- Leading cause of cardiovascular disease (CVD)
- Progressive inflammatory disease of the vascular wall
- Characterised by distinct pathophysiological regions



Proteomic approaches

Hypothesis generating

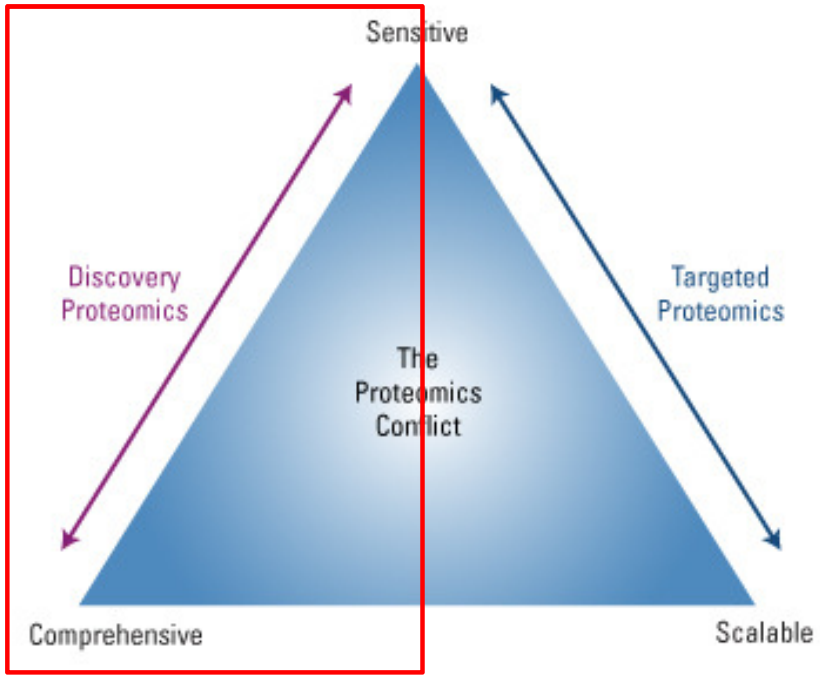


Hypothesis driven

image obtained from ThermoFisher; quantitative proteomics resource library

Proteomics & atherosclerosis research

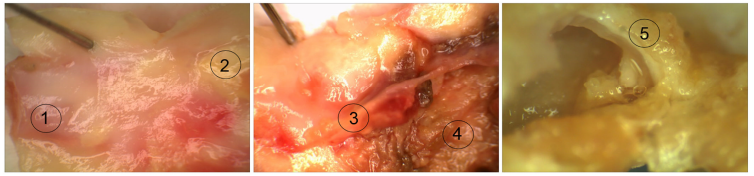
- "proteom* AND athero*" → 876 publications
- + "human" → 674 publications
- + "tissue" → 180 publications



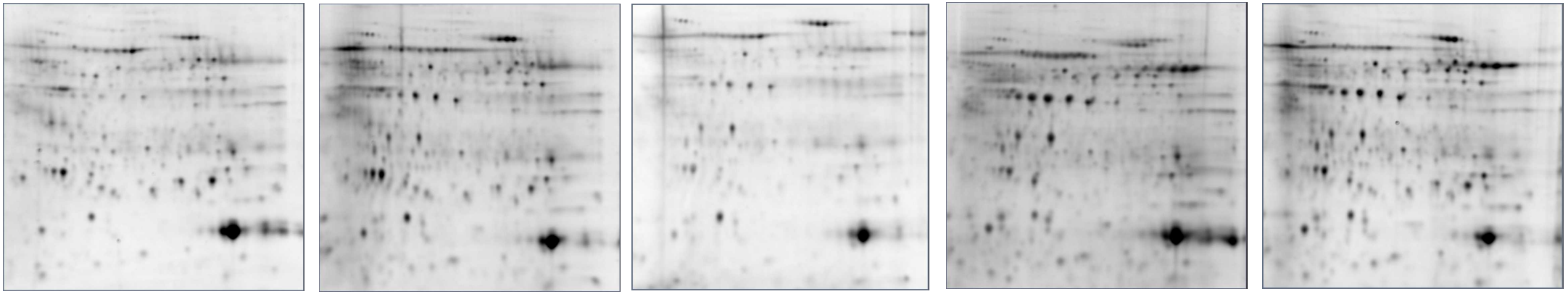
- Discovery proteomics → <30 publications

"Heterogeneity"

Plaque heterogeneity

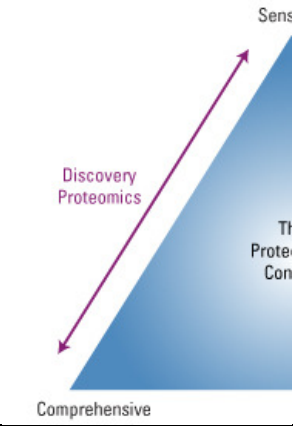


Internal Control | **Fatty Streak** | **Plaque Shoulder** | **Plaque Centre** | **Fibrous Cap**



- Identified 127 spots = 52 proteins
- 15 proteins previously unmapped in atherosclerotic tissue

What more information could we get using tandem-MS?



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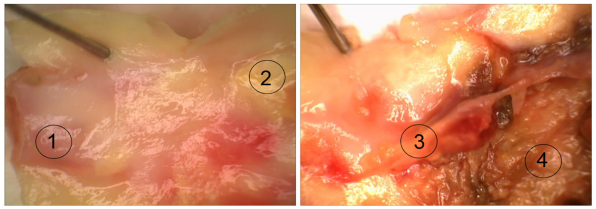
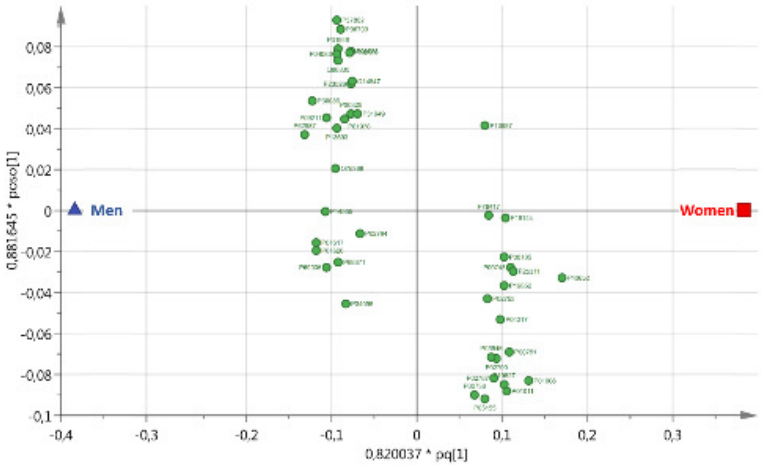
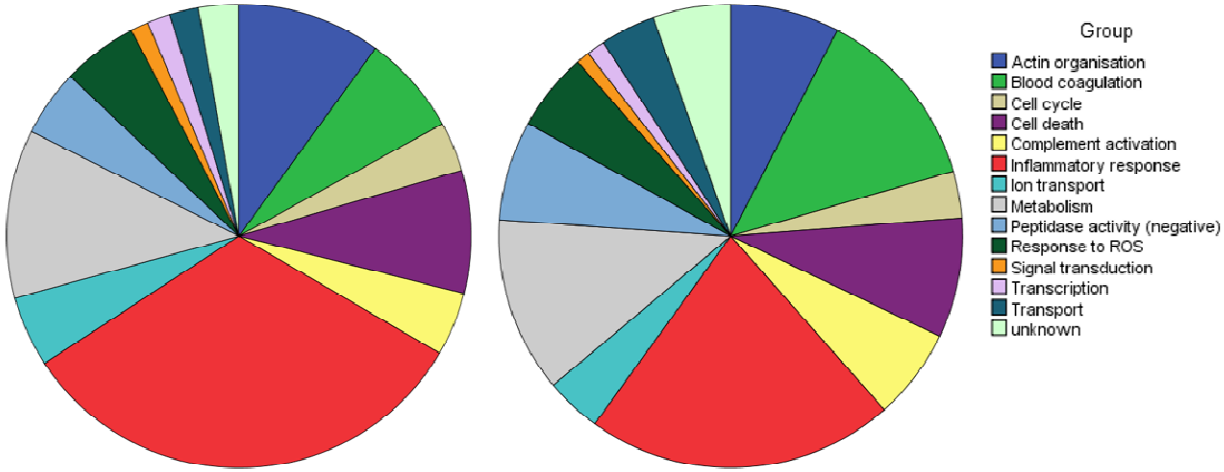
Tandem-Mass Spectrometry





Multivariate statistical modelling
OPLS-DA



Men
n = 10

Women
n = 10

Figures obtained from Ward, et al. *Unpublished*.

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Sex differences – Plaque

Men

- ↑ sPLA2
- ↑ Lysozyme C
- ↑ Ferritin

"Vulnerable Plaque"

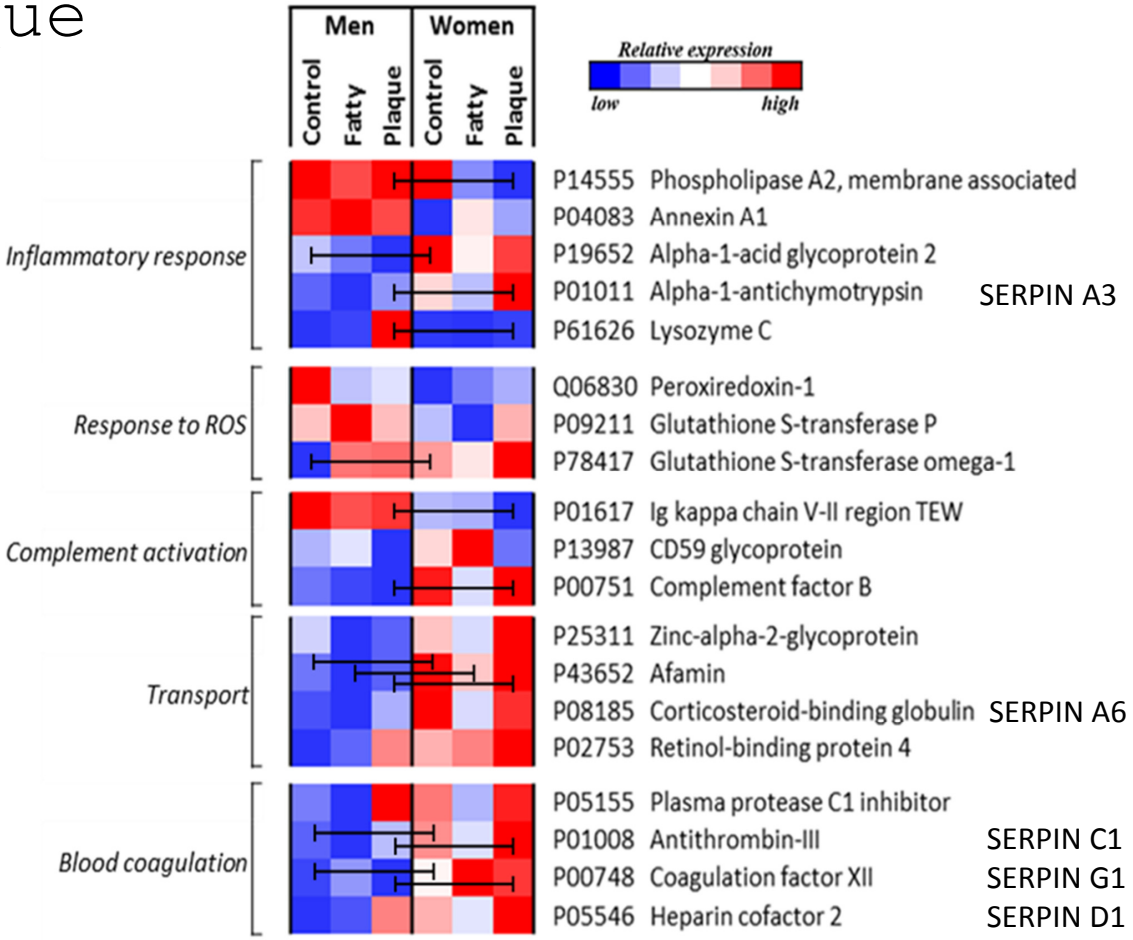
- ↑ inflammation
- LDL hydrolysis
- Foam cell formation

Women

- ↑ SERPINS
  - A3, A6, C1, D1, G1
- ↑ Afamin

"Stable Plaque"

- ↓ inflammation
- Thrombin inhibition

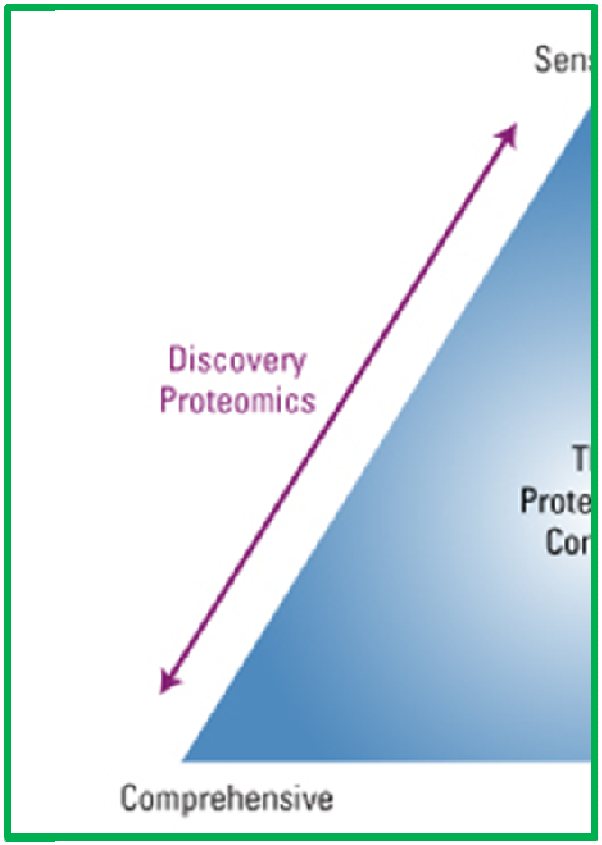


Figures obtained from Ward, et al. *Unpublished*.

Future – our work?

- Expand our current sample cohort
- Metal analysis
- MS-Imaging – combing proteomics and histology

- Plasma proteomics



Other Applications

- Cells
- Plasma
- Nasal lavage
- CSF
- Saliva

Wear Particles from Studded Tires and Granite Pavement Induce Pro-inflammatory Alterations in Human Monocyte-Derived Macrophages: A Proteomic Study

Helen Karlsson[†‡], John Lindbom[†], Bijar Ghafouri[†‡#], Mats Lindahl[†], Christer Tagesson[†‡], Mats Gustafsson[§], and Anders G. Ljungman[*†]

Persistent organic pollutants distribution in lipoprotein fractions in relation to cardiovascular disease and cancer

Stefan A. Ljunggren [a], Ingela Helmfrid [b], Samira Salihovic [c], Bert van Bavel [c], Gun Wingren [a], Mats Lindahl [a], Helen Karlsson [b]

Airway Symptoms and Biological Markers in Nasal Lavage Fluid in Subjects Exposed to Metalworking Fluids

Louise Fornander, Pål Graff, Karin Wåhlén, Kjell Ydreborg, Ulf Flodin, Per Leanderson, Mats Lindahl, Bijar Ghafouri

Published: December 31, 2013 • https://doi.org/10.1371/journal.pone.0083089

Clear differences in cerebrospinal fluid proteome between women with chronic widespread pain and healthy women – a multivariate explorative cross-sectional study

Patrik Olausson, Bijar Ghafouri, Emmanuel Bäckryd, and Björn Gerdle

The proteomic profile of whole and glandular saliva in healthy pain-free subjects

Hajer Jasim, Patrik Olausson, Britt Hedenberg-Magnusson, Malin Ernberg & Bijar Ghafouri

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Jilin University Hospital, China
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University of Alberta, Canada
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Scientific Reports, 2016

Distinctive proteomic profiles among different regions of human carotid plaques in men and women

Wenzhao Liang[1,2,*], Liam J. Ward[1,3,*], Helen Karlsson[1], Stefan A. Ljunggren[1], Wei Li[3], Mats Lindahl[4] & Xi-Ming Yuan[1]

Stroke, 2018

Carotid Atheroma From Men Has Significantly Higher Levels of Inflammation and Iron Metabolism Enabled by Macrophages

Xi-Ming Yuan, MD, PhD*; Liam J. Ward, MSc*; Claes Forssell, MD, PhD; Nabeel Siraj, MD, MSc; Wei Li, MD, PhD