The HDL proteomic in acute coronary syndromes shifts to an inflammatory profile

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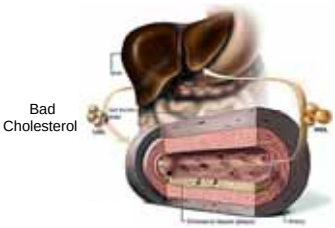
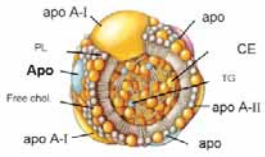
Reverse Cholesterol Transport



High-density lipoprotein or HDL is one of the five major groups of lipoproteins

What is HDL?



What proteins are associated with HDL? Do they change depending on the vascular environment?

The evolution of man?

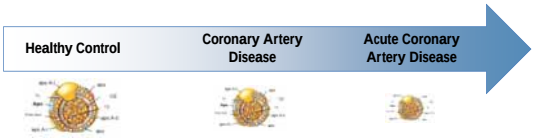


Table 1: Clinical characteristics of study subjects

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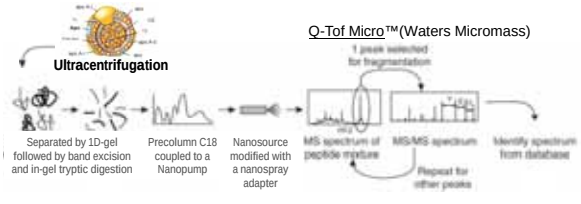
Group	*n*	Age	Cholesterol (mg/mL)	Triglycerides (mg/mL)	HDL-C (mmol/L)	LDL-C (mmol/L)	ApoA-I (mg/mL)	ApoB (mg/mL)	hsCRP
Control	10	51(8)	5.50(1.25)	1.69(0.74)	1.24(0.21)	3.49(1.15)	1.49(0.22)	1.11(0.26)	1.7(1.6)
Stable	10	58(7)	4.75(1.51)	1.46(0.81)	1.06(0.21)	3.09(1.09)	1.40(0.16)	1.21(0.42)	1.4(1.2)
Acute	10	51(10)	3.96(0.26)*	1.41(0.81)	0.75(0.22)*	2.58(0.51)	1.15(0.29)*	0.99(0.10)	30.4(40.1)*

Results represent mean(SD). * P≤0.05 between control subjects and acute or stable coronary artery disease by Student's *t* test.

Control : **Group A**
Stable : **Group B**
Acute : **Group C**

Shotgun proteomics

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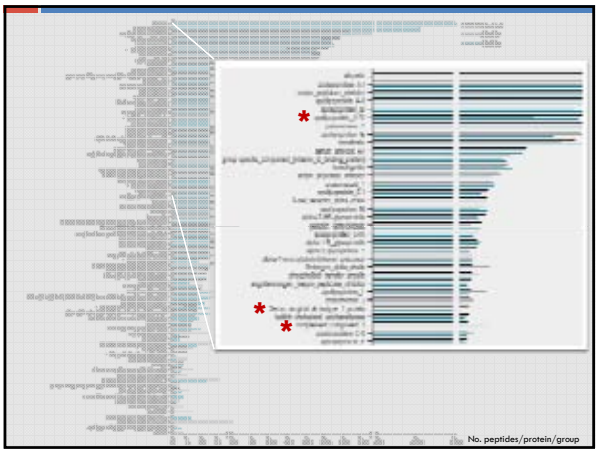
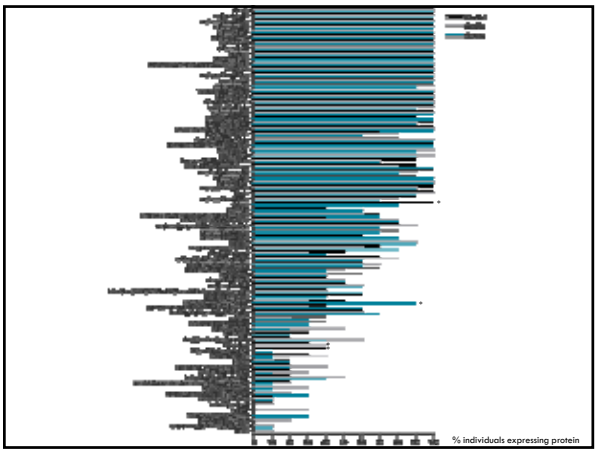
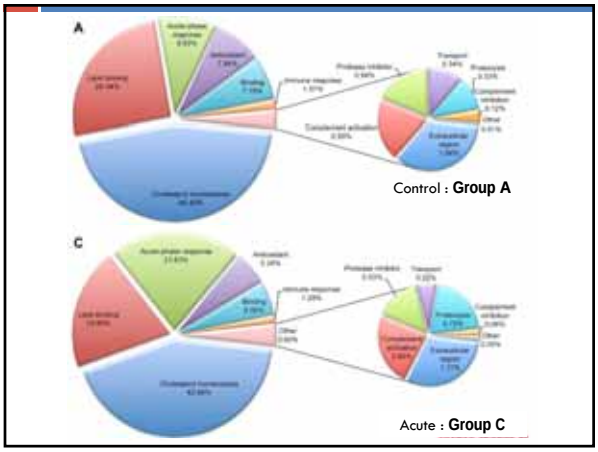
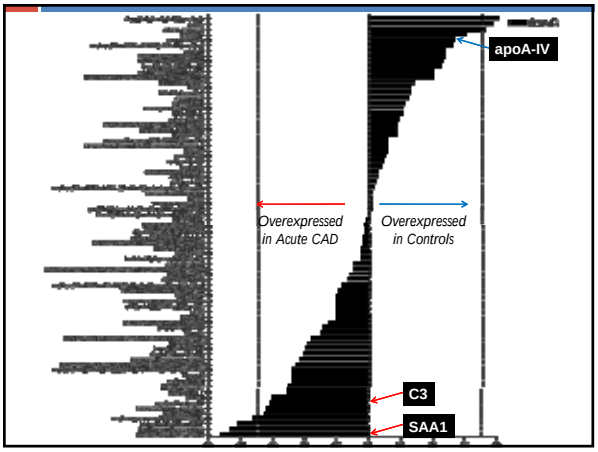
         61 reqlgpvtqe fwdnlekete glrqemskdl eevkakvqpy lddfqkkwqe
emelyrqkve
        121 plraelqega rqklhelqek lsplgeemrd rarahvdalr thlapysdel
rqrlaarlea
        181 lkenggarla eyhakatehl stlsekakpa ledlrqgllp vlesfkvsfl
salefqkkl
        241 ntq
```

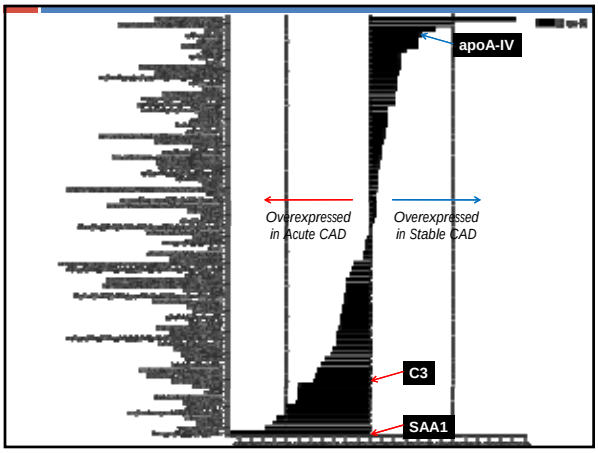
ApoA-I: 13 peptides, seen ~250 times/sample

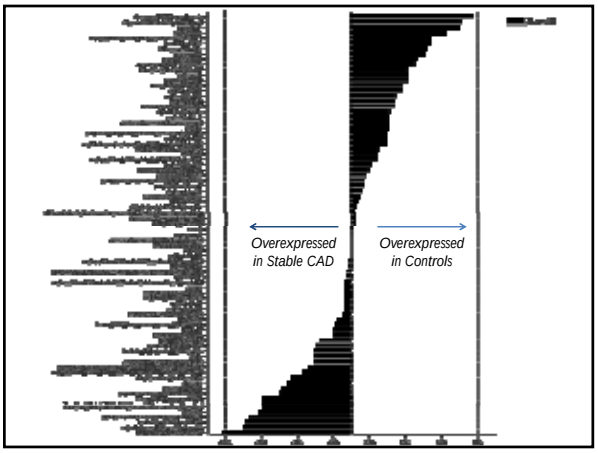

No. peptides/protein/group


% individuals expressing protein


A
Control : Group A
C
Acute : Group C


apoA-IV
Overexpressed in Acute CAD
Overexpressed in Controls
C3
SAA1


apoA-IV
Overexpressed in Acute CAD
Overexpressed in Stable CAD
C3
SAA1

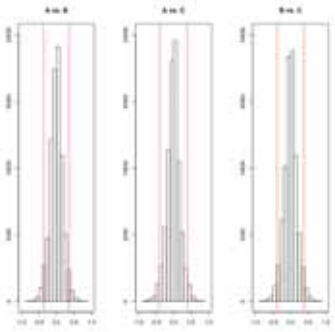

Overexpressed in Stable CAD
Overexpressed in Controls

Peptide index

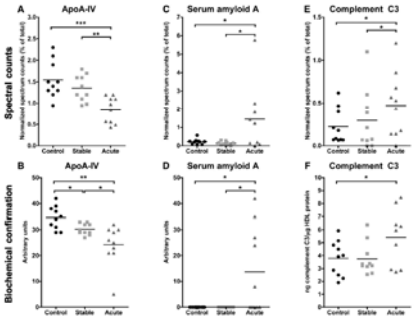
- Semi-quantitative comparison of relative protein abundance between two groups

$$= \left[\frac{\text{Peptides in } \mathbf{Grp1}}{\text{Peptides in } \mathbf{Grp1} + \mathbf{Grp2}} \times \%\ \text{Grp1 subjects with} \geq 1\ \text{peptide} \right] - \left[\frac{\text{Peptides in } \mathbf{Grp2}}{\text{Peptides in } \mathbf{Grp1} + \mathbf{Grp2}} \times \%\ \mathbf{Grp2}\ \text{subjects with} \geq 1\ \text{peptide} \right]$$

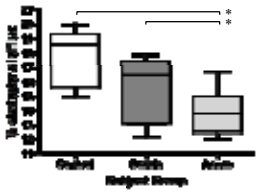
Permutation analysis of peptide index



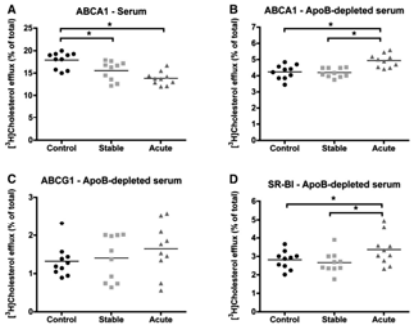
Quantification of protein abundance by spectrum counts and confirmed by immunoblot and ELISA



Macrophage ABCA1-mediated cholesterol efflux assay



ABCA1-mediated cholesterol efflux assay



Summary of findings

- Using shotgun proteomic analysis we have identified 67 proteins associated with HDL
- We have validated 62 previously reported proteins, and reported 5 novel proteins:
  - zinc-α-2-glycoprotein
  - aminopeptidase N
  - Cathelicidin antimicrobial peptide
  - leucine-rich α-2-glycoprotein
  - Carbonic anhydrase I
- We have demonstrated that the composition of HDL changes depending on vascular status