

CORONARY ANGIOPLASTY PRODUCES ALTERATIONS IN THE HDL PROTEOME OF PATIENTS WITH CORONARY DISEASE

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Proteins related to inflammation, complement system regulation, protease inhibition and acute phase have been found associated to HDL. These findings suggest new unknown roles for HDL not related to lipid metabolism. The objective of this study was to investigate whether HDL could be implicated in the reverse transport of proteins and degradation products of the atheroma plaque to remove them from peripheral tissues. We assessed the hypothesis that coronary angioplasty could produce changes in the pattern of HDL-associated proteins.

Plasma before and after surgery were collected from 9 ischemic cardiopathy patients undergoing coronary angioplasty. ApoAI-containing HDL was affinity-purified. HDL-associated proteins were in-gel digested, and peptides were either O¹⁶/O¹⁸ labelled in a pool study or iTRAQ labelled in four subject-to-subject studies. Labelled peptides were fractionated by SCX and identified/quantified by HPLC-MS/MS using a linear ion trap. Results were analyzed with a statistical model developed in our laboratory, using QuiXoT.

We were able to quantify 263 HDL-associated proteins, which is one of the deepest analyses performed in this proteome to date. Statistical analysis yielded a high protein variance between individuals, indicating that HDL protein composition was highly patient-specific. Protein variances within the same individual were considerably lower, indicating that HDL proteome extraction was reproducible and that the vast majority of HDL-bound proteins remained at constant levels. Around 10% of HDL-bound proteins changed their expression levels after angioplasty. Global analysis by systems biology approaches revealed alterations in the pattern of HDL proteins involved in coagulation, acute-phase response, signal transduction and lipid transport. We conclude that although HDL protein composition is highly variable among patients, it shows coherent changes after coronary angioplasty. Our results have important implications for the use of HDL-associated proteins as biomarkers of coronary disease, and support a role for HDL in non-cholesterol reverse protein transport from peripheral tissues.