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## Plasma lipids display increased mean aliphatic chain length in human hypertensive heart disease

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**Purpose:** In Hypertension, left ventricle (LV) hypertrophy (LVH) is a potent prognostic factor to predict outcome. Proton Nuclear Magnetic Resonance (<sup>1</sup>H NMR) spectroscopy, a new technique for analyzing blood metabolites profiles has proved to be one of the most powerful technologies in metabonomic studies of biofluids. We investigated for plasma LVH biomarkers of human Hypertensive Heart Disease.

**Methods:** In this prospective study, 96 hypertensive patients (48 LVH vs. 48 normal LV size) and 24 healthy controls were selected from 2007 to 2009 for plasma <sup>1</sup>H NMR-based metabonomic profiling. A multivariate analysis of the spectral data set was performed by using the Partial Least Squares Discriminant Analysis (PLS-DA).

**Results:** PLS-DA Scores plot of spectral data revealed sample clustering according to the clinical state. PLS-DA loading plot reveals the variables influencing that discrimination which have been identified as signals coming from the methylene (-CH2) and methyl (-CH3) moieties of aliphatic chain from plasma lipids. Thus, the CH2/CH3 ratio which is an indicator of mean length of the aliphatic lipid chain was significantly higher for the LVH group of patients (p<0.01). None difference was observed between two hypertensive groups for blood level of Cholesterol or acyl chain.

**Discussion:** LVH is associated with profound metabolic changes. Indeed, fatty acid (FA) oxidation is lowered in LVH as a consequence of PPAR alpha transcription factor underexpression. In particular, a selective impairment of long chain FA oxidization via a down regulation of CPT1 has been demonstrated in animal models. These observations could explain changes in lipid profiles observed in LVH's group plasma.

**Conclusion:** Thus, the mean length increase of the aliphatic lipid chain we measured in the plasma from LVH patients is in agreement with previous studies on cardiomyocytes that showed a lipid metabolism alteration with a lower oxidation rate for long chain FA.

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# The cardiorenal anaemia syndrome in chronic heart failure: focus on sympathetic activity

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**Objective:** Cardiorenal anaemia syndrome is known to increase mortality and morbidity in patients with CHF. The role of the sympathetic nervous system and related-reflexes in the pathophysiology remains unknown.

**Design and Methods:** The prospective study was conducted at the Intensive Cardiac Care Unit, Rangueil University Hospital, Toulouse, France. We studied 15 patients with CRA syndrome (age: 66.5±3.1 years; mean BMI: 24.12±0.9 kg/m²) and 15 control patients with CHF alone matched for age, gender distribution, type of cardiomyopathy, left ventricular ejection fraction (LVEF) and BMI. We compared sympathetic nerve activity (MSNA), sympathetic baroreflex function (assessed by the slope of the relationship between muscle sympathetic nerve activity (MSNA) and diastolic blood pressure) and its modulation by peripheral chemoreflex, in both groups.

**Results:** Baseline MSNA was significantly elevated in CHF patients with CRA syndrome compared with patients with CHF alone  $(83.1\pm4.6 \text{ versus } 64.9\pm2.9 \text{ bursts}/100 \text{ heart beats; } P<0.01)$  and sympathetic baroreflex function impaired  $(2.69\pm0.44 \text{ versus } 5.25\pm0.60 \text{ %/mmHg; } P<0.01)$ . In comparaison with control, chemoreflex deactivation with administration of 100% oxygen

led to a significant decrease in muscle sympathetic nerve activity and an increase in arterial baroreflex sensitivity in patients with CRA syndrome.

Conclusion: CRA syndrome is associated with elevated sympathetic activity mediated by both baroreflex impairment and tonic activation of peripheral chemoreflex. The latter, through direct interaction with sympathetic baroreflex function subsequently contributes to further activation of the SNS tone. Altogether, mechanisms described in this study could partly explain how CRAS contributes to the progression of CHF and increases morbidity and mortality in these patients.

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# The C93T and G121A polymorphisms of the LPA gene is not associated with susceptibility to acute myocardial infarction

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**Background:** Acute myocardial infarction (AMI) is the clinical manifestation of the chronic development of coronary artery atheroma, with the final process of plaque rupture and coronary thrombosis. Plasma lipoprotein (a) (Lp(a)) levels are mainly genetically determined. The C93T and G121A polymorphisms are a naturally occurring variant of the LPA gene that may influence Lp(a) concentration. The role of Lp(a) in the pathogenesis of myocardial infarction has not been established.

Methods: A one hundred sixty-eight AMI patients compared to 169 healthy controls.

**Results:** No association between LPA C93T genotypes and AMI was found. The frequencies of the GG, GA and AA genotypes of LPA G121A polymorphism were not significantly different in AMI patients and in healthy controls (45.2 %, 48.2%, 6.6 % vs 41.7%, 49.4%, 8.9%, P=0.880). In multivariate logistic regression analysis with covariates including traditional risk factors (diabetes, hypertension, smoking and cholesterol) and, The C93T and G121A polymorphisms, hypertension was independently associated with increased risk of AMI (OR=3.5, P=0.058; OR=0.78, P=0.103 respectively).

**Conclusion:** The C93T and G121A polymorphisms of the LPA gene is not associated with susceptibility to acute myocardial infarction.

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The effect of HDL3-anionic peptide factor on cellular cholesterol efflux and CETP activity in type 2 diabetic patients with and without coronary artery disease

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**Background:** The prevention of atherosclerosis depends on the high-density lipoprotein (HDL) capacity to stimulate the efflux of unesterified cholesterol from cell. The high density lipoprotein Anionic Peptide Factor (HDL3-APF) was previously described as an apolipoprotein that promotes the reverse cholesterol transport. This was demonstrated in vitro conditions and in animal model. On another side, it was shown that reverse cholesterol transport was altered in type 2 diabetes with or without coronary artery disease (CAD).

Patients and Methods: We investigated a possible association between plasma HDL3-APF concentration, cholesterol efflux from Fu5AH cells and cholesteryl ester transfer protein (CETP) activity in type 2 diabetic patients with CAD (n=36), those without CAD (n=20), and 37 healthy subjects as a