hypothesis for a central role of vascular oxidative stress in the development of ASAA.

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CRH regulates cardiac function in normal and inflammatory states

Theodora Tzanvari (1), Aimilia Varela (1), Constantin Puntos (2), Katia Karalis (1), Dennis Kokkinos [Orateur] (1)
(1) Biomedical Research Foundation, Athens, Greece – (2) Medical School, University of Athens, Athens, Greece

The response of various systems to stressful stimuli is influenced by the HPA axis. We investigated the contribution of the stress hormone corticotropin (CRH) to cardiac function in basal and stressful conditions in Crh-null (Crh−/−) and wild-type (Crh+/+) mice. The stressfull inflammatory reaction was induced by LPS, Heart Rate (HR), percentage of LV fractional shortening (FS) and Ejection Fraction (EF) were calculated by echocardiography. At baseline, cardiac function was compromised in Crh−/− compared to Crh+/+ mice, as shown by cardiac hypertrophy, significantly lower FS and EF at 6 and 20h after LPS treatment and more drastically in Crh−/− mice. LPS-treated mice had significantly increased number of apoptotic cells. Their cardiac muscle showed greatly reduced ERK1/2 and Akt phosphorylation and increased levels of MMP13. LPS administration significantly reduced FS and EF at 6 and 20h post-LPS treatment, compared to no mortality among Crh+/+. 100% 16-28h post-LPS treatment, compared to no mortality among Crh+/+. We investigated the contribution of glucocorticoid insufficiency in Crh−/−, corticosterone was replaced for a week prior to LPS treatment, but that improved the effect of LPS on Crh−/− only when accompanied with an acute dexamethasone injection. To our knowledge, this is the first indication of endogenous CRH acting directly in cardiac function and development under basal conditions and as a cardioprotective factor in response to systemic inflammatory stress such as endotoxaemia.

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RANTES/CCL5 exerts pro-angiogenic effects in vitro and in vivo experimental models through the oligomerization and binding to glycosaminoglycans

Nadine Suffee [Orateur]
Inserm U698, Bobigny, France

Atherosclerosis is an inflammatory disease in which the coordination of angiogenesis and inflammation is achieved by the ability of both endothelial cells and monocytes to respond to chemokines. We here address both in vitro and in vivo techniques, the influence of RANTES/CCL5 on angiogenesis, and the role of its cellular ligands CCR1, CCR5, syndecan-1 (SDC-1), syndecan-4 (SDC-4), CD-44 in this effect.

The angiogenic effects of RANTES/CCL5 or its mutants, [E66A] – RANTES/CCL5 with impaired ability to oligomerize, and [°AANA] – RANTES/CCL5 mutated in the main RANTES/CCL5-GAGs binding site were analyzed in vitro in a rat-ecodisc model, and in vivo by measuring angiogenesis in the induction of RANTES/CCL5 cellular ligands such as G Protein-Coupled Receptors and proteoglycans in RANTES/CCL5-induced biological effects.

Our data demonstrate that RANTES/CCL5 is pro-angiogenic both in vitro and in vivo experimental models. This activity depends on RANTES/CCL5 binding to CCR1, CCR5, SDC-1, SDC-4 or CD-44. Moreover, oligomerization and binding to glycosaminoglycans are essential steps in the induction of RANTES/CCL5 angiogenic effects. Altogether our results suggest that the induction of angiogenesis by the chemokine RANTES/CCL5 lead to new therapeutic approaches for reendothelialization after vascular injury.

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Lipoprotein-associated phospholipase A2 (Lp-PLA2) in a population of patients with metabolic syndrome

David Rosenbaum [Orateur] (1), Randa Bittar (2), Dominique Bonnemfent-Rousselot (2), Philippe Girail (1), Xavier Girerd (3), Eric Brückert (1)

Objectives: It has been shown that blood levels of Lp-PLA2 predict future cardiovascular events independently from traditional cardiovascular risk factors. Metabolic syndrome has been associated with an increased cardiovascular risk. The aim of this study was to study the relationship between Lp-PLA2 and metabolic syndrome components.

Methods: Patients were recruited at our outpatient clinic. None should have any history of cardiovascular disease and all underwent routine clinical and biological assessments. Lp-PLA2 was measured in serum with a Plac Test turbidimetric immunoassay.

Results: 148 patients were included with a mean age of 53 years. Lp-PLA2 levels ranged from 41 to 407 ng/mL with a mean of 189 ng/mL (SD: 67 ng/mL). 119 patients (80%) presented with at least 3 NCEP ATPIII criteria of metabolic syndrome and 61 (41%) had treatment for diabetes. 58 patients (39%) were under statin treatment. Our results showed that neither the presence of metabolic syndrome, nor the number of its components influenced Lp-PLA2 levels. We found no individual link between each component of the metabolic syndrome and Lp-PLA2 levels except for diabetes mellitus. There was a negative correlation between diabetes and Lp-PLA2 that did not persist after adjustment for lipid lowering treatments. In univariate analysis, we found a strong linear correlation between Lp-PLA2, LDL-cholesterol (r=0.377 p<0.001). This association existed whereas patients were treated by statins or not. Accordingly, a statin intake was associated with significantly lower Lp-PLA2 levels (190 ng/mL vs. 148 ng/mL, p<0.001). There was no correlation between other traditional risk factors (age, gender, smoking status, blood pressure) and Lp-PLA2 levels.

Conclusion: In our eucaucasan population of patients with metabolic syndrome in primary prevention, we confirmed that Lp-PLA2 levels were totally independent of the components of metabolic syndrome and of any traditional risk factors. In the opposite, they were strongly correlated with LDL-C and statin intake. It highlights the fact that interpretation of Lp-PLA2 assay may need to be adjusted for LDL-C level and lipid lowering therapy to be completely accurate.

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Influence of endothelial nitric oxide synthase gene polymorphisms (894G>T, –786T>C, 4a4b) in Tunisian patients with myocardial infarction

Riadh Jemaa [Orateur] (1), Amani Kallel (1), Youssra Sediri (1), Moncef Feki (1), Mhammed Sami Mourali (2), Salem Abdessalem (2), Rachid Mecheneche (2), Nazila Kaabachi (1)
(1) Hôpital la Rabta, Biochimie, Tunis, Tunisie – (2) Hôpital la Rabta, Cardiologie, Tunisie, Tunisie

Introduction: The 894G>T, –786T>C and 4a4b polymorphisms of the NOS3 gene have been associated with coronary artery disease (CAD) in several populations worldwide, but results are still controversial. In the present study, we examined the association between the 894G>T, –786T>C and 4a4b polymorphisms of the NOS3 gene and myocardial infarction (MI) in a sample of the Tunisian population.

Methods: A total of 303 unrelated patients with MI and 225 controls were included in this study. The 894G>T and 894T>C single nucleotide polymorphisms were analyzed by PC-RFLP, and 4a4b polymorphism by PCR.

Results: The genotype distribution and the relative allelic frequencies for the 894G>T and 786T>C polymorphisms were not significantly different between MI and control subjects (p = NS). Moreover, the odds ratio for MI associated with the 894T (OR = 1.02, 95% CI 0.76-1.35), –786C (OR = 1.09, 95% CI 0.77-1.52).