ASSOCIATION OF PAI-1 4G/5G AND -844G/A GENE POLYMORPHISMS AND CHANGES IN PAI-1/TPA LEVELS IN MYOCARDIAL INFARCTION. A CASE-CONTROL STUDY

N. Abboud 1, L. Ghazouani 1, S. Saidi 1, S. Belhaj Khlifa 1, F. Addad 2, M. Mahjoub 2, Y.-W. Almawi 3, T. Mahjoub 1

1 Faculté de Pharmacie, Monastir, Tunisia
2 Hôpital Universitaire Fattouma Bourguiba, Monastir, Tunisia
3 Collège De Médecine et Sciences Médicales, Manama, Bahrain

Background — Myocardial Infarction (MI) was reportedly precipitated by acquired and inherited risk factors including the G/A and 4G/5G polymorphisms within the promoter of the Plasminogen Activator Inhibitor-1 (PAI-1) gene. Objective — to investigate the association between gene polymorphism of the PAI-1 and MI in Tunisian.

Methods — PAI-1 G/A was genotyped with polymerase chain reaction — restriction fragment length polymorphism (PCR-RFLP) while PAI-1 4G/5G promoter genotype was established by allele specific polymerase chain reaction amplification of genomic DNA. This study was performed in 305 myocardial infarction patients and 328 unrelated healthy controls. All subjects clinical features and PAI-1 and t-PA activity were tested.

Results — There were two polymorphism within the promoter (a G/A single base substitution polymorphism at -844 bp upstream from the start of transcription and an insertion (5G)/deletion (4G) polymorphism at position – 675). Higher frequency of the 4G allele (p < 0.001; O.R. = 1.929), but a lower frequency of the 5G allele (p < 0.001; O.R. = 0.356), were seen in patients vs. controls. The frequencies of the -844G (p < 0.001; O.R. = 0.314) allele was lower than -844A allele (p < 0.001; O.R. = 4.076) in patients versus controls. Furthermore significant elevation in plasma PAI-1 levels (88.43 ± 52.85 ng/ml vs. 62.18 ± 39.31 ng/ml; p < 0.05) was seen among patients.

Conclusion — This study indicates that the risk of MI was notably high in 4G carriers and A carriers with elevated plasma PAI-1, and were associated with reduced t-PA levels.

THE BIOMARKERS OF CORONARY EVENTS STUDY (BIOCORE): FROM PLASMA SAMPLING TO DISCOVERY OF NEW CIRCULATING BIOMARKERS OF ATHEROSCLEROSIS USING DIFFERENTIAL PROTEOMIC ANALYSIS.

O. Meilhac 1, T. Leger 1, D. Lavigne 2, J. Fareh 2, L. Guerrier 3, E. Boschetto 3, O. Laprevote 4, J.-B. Michel 1, L. Feldman 1

1 Inserm Unit 698, Paris, France
2 Sysdiag CNRS FRE3009-Biorad, Montpellier, France
3 Biorad, Paris, France
4 CNRS-Icsm, Gif-sur-Yvette, France

In spite of important therapeutic advances during the last 20 years, coronary atherothrombotic complications are and will remain the first cause of death all over the world. Acute coronary syndromes (ACS) are unpredictable and can lead to sudden death before any medical treatment. The development of new strategies for the screening of patients susceptible to develop an ACS is thus of major interest.

We hypothesized that coronary artery disease, in its stable and unstable forms, is associated with modifications of the concentrations of various circulating proteins (circulating proteome), which could be assessed using a new method for pre-treatment of plasma (equalization) before differential proteomic analysis.

Every step from blood sampling to the proteomic analysis (nature of the tubes used, centrifugation time and speed, conditions of storage etc.) was strictly standardized.

Three groups of 30 patients were studied: non-ST elevation myocardial infarction (group 1), stable angina (group 2), angiographically normal coronary arteries without extra-coronary atherosclerosis (group 3). Five milliliters of plasma from each patient were equalized; this methodology (ProteominerTM, Biorad) is based on a solid-phase ligand library of hexapeptides which provides a potential ligand for every protein in the biological sample, with a limited capacity of binding for abundant proteins, thus allowing enrichment in low abundance proteins/peptides. Various strategies of elution have been used in order to increase the number of peaks/spots detected by SELDI-TOF mass spectrometry and by 2D-electrophoresis, respectively. Several differential peaks are currently being identified.

The screening, prognostic and therapeutic values of the new biomarkers discovered using this novel approach will require further validation, using more straightforward assays (eg, ELISA) in case-control and prospective cohorts of patients with coronary artery disease.

MODULATION OF MACROPHAGE ACTIVATION STATE PROTECTS TISSUE FROM NECROSIS DURING CRITICAL LIMB ISCHEMIA IN THROMBOSPONDIN-1-DEFICIENT MICE

N. Brechot 1, E. Gomez 1, M. Bignon 1, J. Khallou-Laschet 2, M. Dussiot 1, A. Cazes 1, C. Alanio-Brechot 3, M. Durand 1, J. Philippe 1, J.-S. Silvestre 4, N. Van Rooijen 5, P. Corvol 1, A. Nicoletti 2, B. Chazaud 6, S. Germain 1 & 6

1 Inserm U833 — College de France, Paris, France
2 Inserm U872, Paris, France
3 Laboratoire d’Hematologie, Hôpital Bicêtre, AP-HP, Le Kremlin-Bicêtre, France
4 Inserm U567, Paris, France
5 Department of Molecular Cell Biology, Free University Medical Center, Amsterdam, Amsterdam, The Netherlands
6 Service d’Hematologie Biologique A, HEGP, AP-HP, Paris, France

Background — Macrophages, key regulators of healing/regeneration processes, strongly infiltrate ischemic tissues from patients suffering from critical limb ischemia (CLI). However pro-inflammatory markers correlate with disease progression and risk of amputation, suggesting that modulating macrophage activation state might be beneficial. We previously reported that thrombospondin-1 (TSP-1) is highly expressed in ischemic tissues during CLI in humans. TSP-1 is a matricellular protein that displays well-known angiostatic properties in cancer, and regulates inflammation in vivo and macrophages properties in vitro. We therefore sought to investigate its function in a mouse model of CLI.

Methods and findings — Using a genetic model of tsp-1/-/- mice subjected to femoral artery excision, we report that tsp-1/-/-...