contain a variable length fatty acid linked to sphingosine or a related long chain base. In addition to its structural role in the metabolism of membrane building blocks such as sphingomyelin, ceramide plays a critical role in trans-membrane signaling, particularly in response to stress challenges. Hence, ceramide participates in regulating differentiation, proliferation, and programmed cell death of cells. The aim of this project is to elucidate the pathway involving p53 and ceramide in the response of solid cancers to hypoxia, in order to elaborate novel therapeutic strategies for p53-mutated solid tumors. Our preliminary results showed that exposure of HCT 116 p53+/+ colon cancer cells to hypoxia induced G2/M arrest accompanied by p53 overexpression and early ceramide accumulation. However in the absence of p53, HCT 116 cells were unable to arrest efficiently in G2/M, and ceramide accumulation occurred at later time points. Understanding the pathway involving p53 and ceramide in the response of cancer cells to hypoxia is crucial for the development of novel therapeutic strategies for p53-mutated solid tumors.

Morphological Changes of Grafts in Patients Who Died after Coronary Artery Bypass Graft Surgery from Isolated Coronary Heart Disease and Associated with Hypertensive Heart Disease

Ruzanna Petrosyan (Beirut Arab University, Lebanon)

Objectives: Vascular graft failure is one of the most common finding in patients undergoing coronary artery bypass graft (CABG) surgery and still remains the major problem after surgery. The aim of the present study was to investigate features of pathomorphological changes in different type of grafts after CABG in patients with isolated coronary artery disease and associated with hypertensive disease. Material and Methods: Histopathological study was performed on 207 fragments of autopsy sections of autoarterial and autovenous grafts using light microscopy. Results: It is shown that the condition of the vascular wall is depend on hemodynamics leading to degenerative changes of the graft as a result of destructive and proliferative processes in the intima and the middle layer. Active replacement of smooth muscle cells of the media by fibrous tissue and then connective tissues leads to thickness of the vascular wall, stenosis on one hand and on the other hand development of unstable atheromatous plaques. Conclusions: Morphological changes of the venous grafts in patients how undergone CABG and had died after surgery from coronary heart disease associated with hypertensive heart disease were more acute with more aggressive course of atherosclerotic changes with diffuse proliferation of processes and formation of unstable plaques.

Hyperglycemia induces vascular remodeling through modulation of leptin and adiponectin synthesis

Ola El Atab and Ola El Atab (AUB and LU, Lebanon)

Background and Aims: Cardiovascular disease is considered a major cause of death in the diabetic population. Detrimental effects of hyperglycemia are well demonstrated especially those related to vascular damages. Moreover, many recent studies have highlighted the association between vascular complications in diabetes and two adipocytokines: leptin and adiponectin (APN). APN exerts protective effects on vascular remodeling while leptin promotes this phenomenon. The aim of our study was to investigate the molecular mechanisms responsible for hyperglycemia-associated vascular disorders, mediated by APN and leptin synthesis in vascular smooth muscle cells (VSMCs). Methods and Results: Rat aorta organ culture was used to investigate the effect of hyperglycemia on APN and leptin protein expression in VSMCs and the potential involvement of the RhoA/ROCK pathway and caveolae in this expression. Moreover, the impacts of hyperglycemia on reactive oxygen species (ROS) production and changes in actin cytoskeleton dynamics, in VSMCs, were investigated. Western blotting and Immunohistochemistry revealed that 24 hours of exposure to hyperglycemia leads to an increase in APN endogenous protein synthesis in VSMCs, which was prevented by 1 hour pretreatment with the ROCK inhibitor Y-27632 and the cholesterol depleting agent methyl ß-cyclodextrin MßCD. However, the increase in APN synthesis fails to provide vascular protection because of the decrease in APN receptors AdipoR1 and AdipoR2 mRNA expression. In addition, hyperglycemia induces endogenous leptin protein synthesis in VSMCs at early stage (1 hour) through RhoA/ROCK pathway and caveolae, and at late stage (24 hours). Moreover, results showed that 1 hour of hyperglycemia significantly upregulated ROS formation which was potently attenuated by 1 hour pre-treatment with Y-27632 and leptin antibody. However, the 1 hour of pre-treatment with APN slightly reduced hyperglycemia-induced ROS production while the disruption of caveolar structures by MßCD significantly increased this production. In addition, the effect of hyperglycemia on NADPH oxidase4 (Nox4) protein expression in VSMCs was assessed by western blot. Results revealed a significant increase in Nox4 protein expression after 24 hours of exposure to hyperglycemia. In order to investigate the association between Nox activity and APN synthesis; aortas were pre-treated for 1 hour with the Nox inhibitor apocynin then incubated for 24 hours in high glucose conditions. This treatment significantly decreased hyperglycemia-induced APN expression in VSMCs. In addition, the effect of hyperglycemia on actin cytoskeleton remodeling was also investigated. Hyperglycemia for 24 hours induced a significant decrease in the Globular/Filamentous-actin ratio in VSMCs. Pretreating aortas with y-27632 and anti-leptin antibody Ob(Y-20) significantly inhibited the polymerization of globular actin into filamentous actin but no inhibition was detected following the pretreatment with APN. Moreover, Q-PCR revealed that 24 hours of exposure to hyperglycemia significantly increased Cyclophilin A mRNA expression. Finally, pretreating aortas with MßCD didn't inhibit hyperglycemia-induced actin cytoskeleton remodeling but the inhibition of Cyp-A by cyclosporin A prevent this mechanism. Conclusion: Taken together, our data prove that hyperglycemia induces endogenous APN and leptin synthesis in VSMCs through RhoA/ROCK pathway and caveolae. Hyperglycemia also leads to the development of oxidative stress and induces actin cytoskeleton remodeling, favoring vascular remodeling.

The natriuretic system in human salivary gland health and disease: potential use to diagnose early stages of malignancy in salivary glands

Angelo Leone (University of Palermo, Italy)

Angelo Leone1, Alessandro Gulino2, Beatrice Belmonte2,Alice George1, Geagea, Walter Arancio2, Claudio Tripodo2 and Isabelle Miletich3

*1)BioNec, Section of Histology, Palermo University School of Medicine, Palermo, Italy 2) Tumour Immunology Unit, Human Pathology Section, Department of Health Science, Palermo University School of Medicine, Palermo, Italy 3) Craniofacial Development, Tower Wing, Guy's Hospital King's College, London, UK The natriuretic peptide system comprises of three ligands - atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and C-type natriuretic peptide (CNP) - and three receptors, NPR-A, NPR-B and NPR-C. Although the heart is the major source of ANP and BNP, production of ANP has been reported in a number of extra cardiac sites including the salivary glands (SGs). Our immunohistochemical studies show all members of the atrial natriuretic system are present in human adult sub-mandibular SGs in three anatomical locations: the excretory ducts, the blood vessel walls and the peripheral nervous system. It is the first time the natriuretic peptide system is shown to be expressed in the peripheral nervous system. We show this pattern of expression is conserved between mice and humans, which suggests an important role for this system in SG function, possibly as a neurotransmitter or neuromodulator during SG homeostasis. We further identified NPRA expression was elevated in the salivary gland stroma of a number of patients with oral squamous cell carcinoma (OSCC), while NPRA expression was downregulated in SG advanced primary OSCC, suggesting high NPRA levels could be used to diagnose early stages of malignancies in SGs.

Correlates of drug resistant infections in Lebanon: A multicenter retrospective study

Roula Matta and Souheil Hallit (Lebanese University, Lebanon); Rabih Hallit (Usek, Lebanon); Anne-Marie Rogues (Université de Bordeaux, France); Pascale Salameh (Lebanese University, Lebanon)