protein indicated that patients had higher IL-18 level than controls, considered both together (303.76 ± 132.23 pg/mL vs.124.75 ± 15.03 pg/mL, mean ± SD, $P < 0.0001$) and after subdivision in CABG (282.89 ± 79.33 pg/mL, $P < 0.001$) and VR patients(354.79 ± 211.94 pg/mL, $P < 0.01$). Also after classification of the patients in subgroups according to their body mass index (BMI) (normal-weight and over-weight/obese), IL-18 levels were higher than those in control group. **Conclusions:** It seems that although these two different groups of patients had similar increased circulating levels of IL-18, which were independent of the BMI status of the subjects, a different local biology for IL-18 may exist at EAT level.

CVBM5. Interleukin-15, Coronary Arthery Disease and Epicardial Adipose Tissue: Possible Correlation

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Background: The epicardial adipose tissue (EAT) has been shown to increase in obesity and to play a potential role in the development of coronary artery disease (CAD) by secreting different mediators.Interleukin-15 (IL-15) is one of the cytokines expressed by the inflammatory cells located at atherosclerotic plaques.In our study we measured IL-15 plasma level in two groups of patients with different degree of adiposity:1)patients affected by CAD and undergoing coronary artery bypass grafting surgery (CABG); 2) patients without CAD undergoing valve replacement surgery (VR).We also compared gene expression levels of IL-15 and its receptor (IL-15RA) in EAT samples isolated from CABG and VR patients. **Methods:** Blood samples of patients CABG or VR were collected after an overnight fasting to measure IL-15 level by immune-enzymatic assay. IL-15 and IL-15RA gene expression were evaluated on EAT biopsy harvested from CABG and VR patients. **Results:** IL-15 plasma level resulted higher in CABG than in VR patients (3.70 ± 1.17pg/mLvs.2.52 ± 1.04 pg/mL; mean ± SD; $P < 0.05$).After classification according to BMI, IL-15 level resulted higher in overweight/obese (OB) CABG compared to OB VR patients (4.54 ± 0.30 pg/mL vs.2.18 ± 0.52 pg/mL; $P < 0.01$). A trend of increase was also observed in normal-weight (NW) CABG compared to NW VR patients (3.58 ± 0.40 pg/mL vs.2.63 ± 0.08pg/mL). Only in CABG group IL-15 level was higher in OB than in NW group (4.54 ± 0.30pg/mL vs.3.58 ± 0.40 pg/mL; $P < 0.001$). **Conclusions:** The increased IL-15 circulating level observed in CABG vs. VR patients seemed more correlated to the CAD pathology than to the obesity status of the patients. Whether EAT may significantly contribute to increase IL-15 circulating levels in these patients need further investigation.

CVBM6. Pathophysiological Implications of Inflammation and Genetic Inflammatory Factors in Hypertensive and Old Patients Affected by Sporadic Thoracic Aortic Aneurysm

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Background: Sporadic thoracic aortic aneurysm (S-TAA) is potentially devastating with severe morbidity and mortality. Current evidence suggests inflammation as main mechanism of its pathophysiology associated with both aging and age-related hypertension. Thus, we assessed whether inflammation is the principal mechanism of medial degeneration in hypertensive and old S-TAA. **Methods:** Histopathological and immunoistochemical aorta examination was executed. Furthermore, genotyping of ten SNPs in cases and controls was performed. Plasma inflammatory molecules were also detected in patients and controls using ELISA technique. **Results:** A significant inflammatory/immune CD3+CD4+CD8+CD58+CD20+ cellular infiltrate mainly in vasa vasorum of adventitia was observed in case aortas, suggesting its possible migration from these vessels into media and its role in destroying all components of extracellular matrix and vascular smooth muscle cells (VSCM)s. Consistent with these data, significant higher plasma levels of systemic inflammatory mediators characterized the cases. Different aorta abnormalities, apoptosis of VSCMs and severe MMP-9 amounts were also found in S-TAA aortas. In addition, five very significant associations with S-TAA risk were detected. Of these, D/I ACE and -1562 C/T MMP-9 SNPs are independent risk factors for S-TAA. Higher tissue and plasma levels of MMP-9 were also observed in -1562T MMP-9 allele carriers. A high S-TAA risk genotype was also detected significantly associated with high levels of systemic inflammatory mediators, immune/inflammatory cells and hypertension. **Conclusions:** Results obtained agree emerging evidence of inflammation as shared pathological mechanism for S-TAA, suggesting the role of inflammatory products and genetic profile as possible S-TAA risk biomarkers.

CVBM7. Role of Oxysterols in the Progression of Atherosclerotic Lesions

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Background: Atherosclerosis has been associated with chronic inflammation which contributes to atherosclerotic plaque progression and rupture. Matrix metalloproteinases (MMP), secreted mainly by macrophages, play a major role in the extracellular matrix remodeling. Dysregulation between MMP and tissue inhibitors of metalloproteinases (TIMP) can render the plaque vulnerable. Increased MMP-9 expression has been found in atherosclerotic plaques of patients experiencing cardiovascular diseases. An association between oxidized LDL and coronary heart disease has also been demonstrated. Oxysterols, cholesterol oxidation products which are abundant in oxidized LDL, appear to be involved in the pathogenesis of atherosclerosis. **Methods:** Human promonocytic U937 cells were treated with an oxysterol mixture, whose composition is similar to that found in human plaques. MMP-9, TIMP-1/TIMP-2 expression was measured by real time RT-PCR whereas MMP-9 and TIMP protein levels were analyzed by Western blotting; MMP-9 enzymatic activity was analyzed by zymography. The production of reactive oxygen species (ROS) was observed by confocal microscope. **Results:** Our results show that the oxysterols induce a significant increase of expression, synthesis and enzymatic activity of MMP-9, whereas they don't affect the expression and synthesis of the inhibitors TIMP-1/TIMP-2. Using inhibitors or specific siRNAs, we demonstrated that oxysterols induce MMP-9 expression through: 1) PKC-mediated NADPH oxidase- and mitochondria-dependent ROS overproduction; 2) up-regulation of ERK1/2 and JNK signaling pathways; 3) up-regulation of AP-1- and NF-κB-DNA binding. Moreover, oxysterols induced inflammatory cytokine expression which might contribute to plaque vulnerability by inducing MMP-9 expression. **Conclusions:** In conclusion, oxysterols significantly contribute to the plaque vulnerability by promoting MMP-9/TIMP-1/2 imbalance in phagocytic cells.

CELL DEATH PATHWAYS

CDP1. Magnesium and its Mitochondrial-Specific Channel (mrs2) in Doxorubicin-Induced Apoptosis of Mammary Epithelial Cells

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Background: Several apoptotic stimuli induce a magnesium release from mitochondria that seems to be functional to the apoptotic process. Mitochondrial RNA splicing gene 2 (*mrs2*) trascribes a channel protein, homologous to the bacterial CorA, which mediates a membrane potential-driven magnesium uptake into mitochondria. Interestingly, mrs2 expression has been associated to tumour multidrug resistant phenotype, although the mechanism remains unclear. We here investigated the role of mrs2 in doxorubicin-induced apoptosis in mammary epithelial cells. **Methods:** Mammary epithelial cells (HC11) were adapted to grow in low or high magnesium medium. Control HC11, high-Mg and low-Mg HC11 were assessed for sensitivity to doxorubicin-induced apoptosis (annexin-fitc, mitochondiral membrane potential and cytochrome c release) and mrs2 expression (Western blot). mrs2-siRNA cells were assessed for doxorubicin sensitivity and compared to wild type counterparts. **Results:** Our results show that sensitivity to doxorubicin depends on magnesium availability. High-Mg cells and magnesium-supplemented HC11 cells (10mM for 48h) are more resistant to doxorubicin-induced apoptosis. Interestingly, in both cell lines mitochondrial mrs2 protein was up-regulated compared to control or untreated cells. Silencing of the *mrs2* gene enhanced doxorubicin-induced apoptosis in all cells. **Conclusions:** Our data suggest that increased magnesium availability protects HC11 cells from doxo-induced apoptosis. The expression of the mitochondrial protein mrs2 is involved in apoptosis resistance as mrs2-siRNA increased doxo sensitivity also in high-magnesium cells. Since mrs2 overxpression has been associated to multidrug resistance (Chen, 2009) we hypothesise that mrs2 and the associated mitochondrial magnesium uptake have a crucial role in the mechanism of drug resistance.

ENDOCRINE AND METABOLIC DISORDERS

EMD1. Novel Mutations in SAR1B and *MTTP* Genes in Children with Chylomicron Retention Disease and Abetalipoproteinemia

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Background: Monogenic hypobetalipoproteinemias (mHBLs) include Familial Hypobetalipoproteinemia (FHBL) with a dominant transmission and