Results: At admission, patients with heart failure showed low-level of serum and urinary sodium. They also showed high plasma levels of ANP, BNP, TNP-α, IL-1β, and IL-6. After 8 days of treatment with high dose furosemide and small volume of HSS, patients with AIVD or CHF showed a significant increase of daily diuresis and urinary sodium, a significant lowering of weight, SBP HR and of ANP, BNP, IL-1β, TNP-α, IL-6 plasma values. Until the end of treatment period was reached, after the acute saline load, patients with CHF or left ventricular dysfunction showed higher, though not statistically significant, plasma levels of ANP and significantly higher plasma levels of BNP, IL-1β and TNP-α, in comparison with values observed immediately after the treatment period in the same patients, nevertheless these plasma values remained lower in comparison with admission values. Moreover, patients with HF treated with IV high dose furosemide + HSS showed, after acute saline load, a lower absolute change of ANP, BNP, TNP-α, IL-1β, IL-6-E-Selectin, V-Selectin plasma levels with respect to the values observed, in the same patients, at the end of treatment period in comparison respectively to the absolute change observed in control subjects (healthy and AIVD subjects), after a saline load, whereas no significant difference was observed between cases and controls in absolute change of IL-10, ICAM-1 and V-ICAM-1 plasma levels.

Conclusion: Treatment with high dose furosemide and HSS, by lowering volume overload could be responsible for a stretching relief that could influence natriuretic peptides and immunoinflammatory marker plasma levels after treatment and after an acute saline load.

35 EFFECT OF A PEPTIDE MAGIC BASED ON THE DIMERIZATION DOMAIN OF THE ID1 PROTEIN ON SMOOTH MUSCLE CELL PROLIFERATION, MIGRATION AND DIFFERENTIATION

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Proliferation and migration of smooth muscle cells (SMCs) are prominent features of atherosclerosis. Among several mediators to be involved in these cellular events, recent evidence indicates a role for the class of transcription factors Helix-Loop-Helix (HLH). E2, E47 and MyoD belong to this family and directly regulate SMC proliferation and migration by inducing the expression of the marker for the contractile phenotype α-actin, and the cyclin-dependent kinase inhibitors, p21 and p16. Within the HLH family members, the protein Id acts as inhibitors of the gene transcription leading to cell-cycle progression and cell de-differentiation. Thus, the proteins Id may represent pivotal players in the development of lesions of atherosclerosis and a potential pharmacological target. In order to modulate their activity, we have designed an interfering molecule (compound 1a and 1b having the same structure but different chirality) containing two copies of the first eleven residues of the Id1 helix-2 (Id1 91–101), which are N-terminally connected through an unnatural dicarboxylic acid c i s 3-carboxycyclopentylglycine (Cpg). To investigate the effect of compounds 1a and 1b on cell proliferation, cultured SMCs from thoracic aorta have been synchronized at the G0 phase of the cell cycle and then stimulated for 3 days with medium containing 10% fetal calf serum (FCS) in the presence or absence of the peptides. 1a and 1b have shown a similar antiproliferative effect by reducing the number of cells to ~60% in the low-micromolar range (~2 μM). An equimolar mixture of 1a and 1b was able to specifically decrease cardioproliferation, thus excluding any relevant role of the conformation of the three chiral centres. The effect on cell migration was performed by pre-incubating the cells with 1 μM or 10 μM of each compound for 24 hours and then treated with a modified Boyden chamber in response to 20 ng/ml PDGF-BB (platelet derived growth factor) as chemotactic agent. A moderate, but still significant, reduction of cell migration was observed at both 1 and 10 μM concentration (~30%). The ability of the Cpg-containing peptides to convert the dedifferentiated state of the SMCs into a differentiated one was evaluated by measuring the expression level of α-actin. A positive response on the expression levels of α-actin has been observed upon incubation of the cells with 10 μM concentration of compound 1a (180 ± 11%). In contrast, the Cpg-containing peptide (1a-cis) displaying two copies of a scrambled sequence of Id1 91–101 did not affect the α-actin expression. Finally, to determine whether the observed modulation of 1a/b on SMC proliferation, differentiation and migration was effectively correlated in the modulation of the Id1 protein activity, we evaluated its intracellular levels. Compound 1a significantly reduced the Id1 level by 65%. This effect may indicate that the conversion of the synthetic phenotype of the SMCs to a contractile phenotype upon incubation with 1a/b may be due to a reduced activity of the Id1 protein. In conclusion, the present study provides evidence on a possible pharmacological modulation of protein Id1, by compound 1a/b which regulates the proliferation, the migration and the differentiation of SMCs.

36 EFFECT OF CIGARETTE SMOKING ON CAROTID IMT AND FRS

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Objective: To investigate 1) whether smokers and non-smokers with identical Framingham risk score (FRS) have a different subclinical vascular damage and 2) whether moderate cigarette smoking throughout the life (in terms of pack-years, a measure of total exposure to cigarette smoking not considered in the FRS) may be considered harmless as compared to the effects of heavy cigarette smoking on the extent of sub-clinical atherosclerosis.

Methods: Carotid IMT of never-, moderate- (pack-years=30) and heavy-smokers (pack-years>30), matched for age, gender and FRS, were compared (n=72 per group).

Results: As a result of the FRS-matching, moderate- and heavy-smokers were fully comparable for all the vascular risk factors (VRFs) included into the algorithm. In contrast, never-smokers had, consequently to the matching, higher levels of total and LDL-cholesterol, blood glucose, systolic and diastolic blood pressure (all p<0.05). The IMTmax of both heavy (1.05±0.31 mm) and moderate smokers (1.02±0.27 mm) was significantly higher than in FRS-matched never-smokers (0.92±0.28 mm, p=0.01 and p=0.003, respectively). Thus, regardless of a moderate or heavy smoking history, smokers show a worse carotid atherosclerotic profile than FRS-matched never-smokers.

Conclusions: Moderate cigarette smoking, whatever moderate or heavy, induces a vascular damage that exceeds that observed in never-smokers matched for FRS, which reveals the particularly strong atherogenicity of this risk factor.Moderation, as defined in this study, may not be considered a harmless alternative to smoking cessation.

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37 ASSOCIATION BETWEEN SMALL DENSE LDL AND CAROTID ARTERIAL EVENTS IN FAMILIAL COMBINED HYPERLIPIDEMIA

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Introduction: The association between small dense LDL and cardiovascular events was evaluated in a group of patients (mean age 46.3 ± 12.5 years) with Familial Combined Hyperlipidemia (FCHL) recruited in the outpatient Lipid Clinic of the "Federico II" of Naples.

Methods and Results: Small dense LDL were determined in 102 probands with FCHL and 146 normolipidemic, normotensive, normoglycaemic healthy subjects. LDL particle separation was performed by Lipoprint System: seven LDL subfractions were obtained and LDL score (% of sd-LDL particles) calculated. In the group of FCHL patients 62.7% had cardiovascular events. The association between sd-LDL and cardiovascular events was evaluated taking into account different adjustment models. Patients with elevated levels of LDL score (above the 90th percentile of control population), showed the following OR of having cardiovascular events: 3.58, 95% Confidence Interval 1.19-10.76, p=0.023; unadjusted. 4.51, 95% Confidence Interval 1.18-17.16, p=0.027; adjusted for age, gender, BMI, HDL, triglycerides. 6.56, 95% Confidence Interval 1.54-27.88, p=0.011; age, gender, presence of Metabolic Syndrome (MS).

Conclusion: This finding shows that this group of patients with LDL score above the 90th percentile of control population (score>10.09) is associated with presence of cardiovascular events. The association of cardiovascular events with small dense LDL is also independent of BMI. Insulin resistance and MS status.

38 EFFECTS OF WEIGHT MODIFICATION ON H5-CSR IN A COHORT OF MEDITERRANEAN WOMEN: FINDINGS FROM PROGETTO ATENA

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Weight modification (Δ weight) in comparison to weight reported at 20 years of age and high sensitive C reactive protein (hs-CRP) were evaluated in a population-based cohort study in women, aged 30-69, living in the metropolitan area of Naples, Southern Italy (Progetto ATENA).