Methods: Embryonic stem (ES) cells were induced to differentiate into SMCs.

Results: miR-22 was significantly up-regulated during SMC differentiation from ES cells. Enforced expression of miR-22 by its mimic, while knockdown of miR-22 by its antagomiR, promotes or inhibits SMC differentiation from ES cells, respectively. Moreover, miR-22 overexpression in stem cells promoted SMC differentiation in vivo. MECP2 was predicted as one of the top targets of miR-22 by several computational miRNA target prediction tools. Interestingly, the expression levels of MECP2 were significantly decreased during SMC differentiation, and MECP2 was dramatically decreased in miR-22 overexpressing cells, but significantly increased when miR-22 was knocked down in the differentiating stem cells. Importantly, luciferase assay showed miR-22 substantially inhibited wild type, but not mutant MECP2-3'UTR-luciferase activity. In addition, modulation of MECP2 expression levels affects multiple SMC-specific marker gene expression in differentiated ES cells. Importantly, our data showed that MECP2 could transcriptionally regulate SMC gene expression through direct binding to promoters of SMαA and SM22α genes, and revealed that the binding sites for serum response factor in SMC gene promoters was responsible for MECP2-mediated SMC gene expression. Finally, H3K9 tri-methylation around the promoter regions of the SMC genes was also found to be significantly increased by MECP2 overexpression.

Conclusion: miR-22 plays an important role in SMC differentiation, and epigenetic regulation through MECP2 is required for miR-22 mediated SMC differentiation.

17 - Gene expression

EAS-0687.

A POLYMORPHISM IN THE GENE FOR PROTEIN TYROSINE PHOSPHATASE 1B IS ASSOCIATED WITH ALTERED LIPID PROFILE AND MYOCARDIAL INFARCTION

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Objectives: To investigate the effect of the Protein Tyrosine Phosphatase non-receptor Type 1 (PTPN1) 1484InsG polymorphism on risk of myocardial infarction (MI) and on levels of intermediate phenotypes related to MI. Heterozygotes for this polymorphism have been previously associated with an altered lipid profile.

Methods: Samples were 524 men with a history of MI (cases) and 628 controls who participated in the Study of Myocardial Infarction Leiden (SMILE). The PTPN1 1484InsG polymorphism was tested by PCR followed by restriction enzyme digestion. Median levels of PTP1B mRNA in blood were measured by multiplex ligation-dependent probe amplification (MLPA), total and HDL cholesterol and triglycerides were calculated for each genotype in controls.

Results: The allele frequency of PTPN1 1484InsG was 7.5% in controls and 6.5% in cases. The age-adjusted odds ratio of MI was 0.9 (95% CI 0.6-1.2) for heterozygotes. This decreased to 0.5 (95% CI 0.3-1.0) following restriction to men 50 years or older who were also smokers. The polymorphism had no effect on PTP1B mRNA expression in the whole group of controls taken together but expression was higher in heterozygote smokers of 50 years or more. Amongst controls, heterozygotes for the PTPN1 1484InsG polymorphism had lower HDL-cholesterol (1.18 vs 1.31 mmol/l, p<0.01) and higher triglyceride (1.44 vs 1.21 mmol/l, p<0.01) levels compared to homozygous wildtype individuals. Quartiles of expression of PTP1B mRNA levels were not associated with levels of total or HDL-cholesterol, or triglycerides).

Conclusion: PTPN1 1484InsG is associated with a lower odds ratio for MI in older men who are also smokers. As reported in other studies the PTPN1 1484InsG polymorphism is associated with lower HDL-cholesterol and higher triglyceride levels. Smoking and age may modify the effect of this polymorphism.

EAS-0713.

COMPLEMENT FACTORS ARE ASSOCIATED WITH BMI AND HOMA-IR

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Objectives: Low level of chronic inflammation is associated with increased BMI, obesity and metabolic disease. There are some factors of the complement pathway that are involved in the chronic inflammation, such as molecules which have a dual role between the immune system and the metabolic system and their function is tissue dependent. Therefore, we consider the analysis of some of the components of C3 complement, the adipin and the CS2 receptor in patients with different degrees of obesity and metabolic disease.

Methods: We studied 89 subjects with different BMI levels. Measurements of anthropometric and biochemical variables were done. Samples of visceral adipose tissue were obtained during bariatric surgery in the morbidly obese patients or hiatal hernia surgeries in the rest of patients. The RNA isolation from adipose tissues was done using RNAeasy Lipid Tissue Mini Kit and the gene mRNA expression levels were assessed by real-time PCR using an ABI Prism 7500 Sequence Detection System.

Results: We showed a positive correlation of CS2 with the BMI, the waist circumference and HOMA-IR, while the adipin only correlates with the BMI. Moreover, we have found a different gene expression levels in subjects with different BMI, showing a higher CS2 and adipin expression levels in the morbid obesity patients compared with the low weight subjects.

Conclusion: There is a greater expression level of inflammatory genes in the adipose tissue of morbid obese patients.

17 - Gene expression

EAS-0996.

EXPRESSION OF ABCA1 AND MMP-9 IN M-CSF MACROPHAGES IS ASSOCIATED WITH ATHEROSCLEROSIS DEVELOPMENT

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