GALECTIN-2 EXPRESSION IS DEPENDENT ON THE 3279C>T POLYMORPHISM AND IS ASSOCIATED WITH ARTERIOGENESIS IN PATIENTS WITH CORONARY ARTERY DISEASE

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Background: Arteriogenesis is a potent natural defense mechanism that protects the myocardium from ischemic damage in patients with a coronary artery disease. Monocytes/macrophages are known to be important modulators of this process. In the present study, we investigated the transcriptome of the circulating monocytes of patients with a total coronary occlusion to find targets that are important for arteriogenesis.

Methods: A total of 50 patients with a chronic total coronary occlusion were dichotomized according to their collateral flow index (CFI), which is the golden standard to measure the capacity of the collateral circulation. From each patient, RNA was isolated from unstimulated peripheral blood monocytes, monocytes stimulated by lipopolysaccharide (LPS), or from monocytes after differentiation into macrophages. Whole genome transcriptome analysis was performed in carefully matched patients from both ends of the CFI spectrum and analysed by pathway-based bioinformatics. The expression of genes of interest was validated using RT-PCR. Galectin-2 intron 1 3279C>T was typed by HpyCH4IV digestion of PCR products.

Results: Genome-wide mRNA expression analysis confirmed our previous findings of enhanced Interferon-beta signaling in patients with low CFI. Interestingly, increased expression of Galectin-2 was observed in all three cell types from patients with low CFI, as compared to the patients with high CFI. This observation could be confirmed by RT-PCR (p=0.01 for the resting monocytes; p= 0.05 for the LPS stimulated monocytes; p=0.02 for the macrophages). In vitro effects of Galectin-2 on several cell types involved in arteriogenesis were studied. Importantly, we found that the expression of Galectin-2 was associated with the Galectin-2 intron 1 3279C>T single nucleotide polymorphism (SNP), a transcriptional regulatory SNP that has previously been reported to be associated with myocardial infarction.

Conclusions: The results of the present study suggest that Galectin-2 and the Galectin-2 intron 1 SNP, as a regulator of Galectin-2 expression, have an important role in arteriogenesis.