**THE NOVEL SMALL LEUCINE RICH-REPEAT PROTEIN PODOCAN IS A SELECTIVE SYSTEMIC AND LOCAL REGULATOR OF SMOOTH MUSCLE CELL FUNCTION VIA THE CANONICAL WNT-PATHWAY: LESSONS LEARNED IN MICE AND MEN**

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Smooth muscle cell (SMC) function critically influences the clinical course of vascular disease. The close regulation of SMC migration and proliferation within the intimal space is critical in maintaining a delicate balance between insufficient and excessive atherosclerotic plaque repair. When SMC proliferation is too suppressed, the ensuing weakening of the fibrous cap can result in plaque vulnerability and acute coronary syndrome. Podocan is a protein within the Single Leucine Rich-Repeat (SLRP) protein family. Podocan was shown by our group to be a potent negative regulator of the migration and proliferation of both murine and human SMCs. This effect was mediated by downregulating Wnt-pathway activity in SMC. The Wnt-pathway has increasingly been implicated in regulating activity of SMC. To test the possible role of Podocan as a new biomarker to predict coronary risk we designed a prospective clinical trial with the following specific aims: Specific Aim 1 was to study the association between podocan, CRP-1, and Dkk-1 and acute coronary syndrome (Unstable angina, NSTEMI, STEMI), comparing patients undergoing cardiac catherization for ACS with stable obstrutive CAD and non-coronary chest pain. At enrollment at the time of baseline cardiac catherization, angiographic SYNTAX-score was calculated. Specific Aim 2 was to assess the predictive value for these variables for the recurrence of ACS over the course of 2 years and for adverse outcome (MI, CVA or death); Specific Aim 3 was to identify a subgroup of premature ACS presentation with low risk factor profile (one or less CAD risk factors), and to compare to our study groups described in Specific Aim 1; We established a strong association of Podocan with Acute Coronary Syndromes and with a subgroup of obstructive CAD with a high SYNTAX-score (>20). We also found a stronger positive predictive value of podocan for MACE-events than for CRP-1 and a cluster of increased circulating podocan levels in non-diabetic patients with increased BMI in premature CAD. These findings suggest a role for podocan as a biomarker in assessing clinical risk in chest pain patients and as a possible target for future novel pharmaco-therapies for unstable CAD.