Pharmacology, Greifswald, Germany

Gene expression of the newly discovered adipokine chemerin is the IFNβ expression in the heart
collected hearts were performed. Hearts were infected with CVB3 for 8 days. Plaque assays and immunohistochemistry of hearts. IFNβ PCR. Fibroblasts were isolated from wildtype (wt) and PAR2 knockout (ko) mouse

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fibroblasts significantly decreased the IFNβ expression. Furthermore, an overexpression of PAR2 in PAR2 deficient cardiac fibroblasts. Furthermore, an overexpression of PAR2 in PAR2 deficient cardiac fibroblasts significantly decreased the IFNβ expression. The negative regulation of IFNβ expression by PAR2 was dependent on a physical interaction between PAR2 and TLR3. The differential IFNβ expression led to a very mild course of myocarditis in PAR2ko mice compared to wt mice. The virus titre was reduced in PAR2ko compared to wt hearts 8d post infection (virus titre wt: 6.8E+06 PFU/ml vs PAR2ko 6.3E+05 PFU/ml, p<0.05) and hematocrit and esin staining revealed strong infiltration of immune cells in infected wt hearts but not in infected PAR2ko hearts.

Conclusion: The myocardial PAR2 expression is negatively associated with the IFNβ expression in human and mouse. Therefore, a reduction of PAR2 protects the heart from myocarditis and increases the IFNβ response.

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Gene expression of the newly discovered adipokine chemerin is modified by inflammatory agents and insulin in cultured cardiomyocytes
D. Rodriguez-Penas, S. Feijoo-Bandin, V. Garcia-Rua, A. Mosquera-Leal, J.R. Gonzalez-Juanatey, M.F. Lago. IDIS, University Clinical Hospital, Santiago de Compostela, Spain

Purpose: Chemerin is a novel adipokine with dual roles in metabolism and inflammation. Our aim was to determine the effects of the mediators TNF-α, desaminethasone and insulin, of exercise and of the delay in the weaning on chemerin gene expression at cardiac level.

Methods: Real-time PCR and western blot was used to investigate mRNA and protein chemerin levels in rat cardiomyocytes treated with TNF-α (0.1-20ng/ml), dexamethasone (0.1-100nm) and insulin (0.1-100nm) for 24h-20 Sprague Dawley male pups were weaned normally at day 21 and other 20 rats were allowed to remain with their mothers until day 28. After the weaning in both groups 10 rats were fed with high fat food (40%) and the other 10 rats with a standard food (31%fat).Four week-old male Sprague Dawley rats were randomly divided into two groups: Control animals (n=11) were allowed free access to food and water, and the exercise group was allowed free access to food, water and the treadmill for 3 weeks.

Results: Real-time PCR analysis showed that TNF-α induced a dose-dependent increase in chemerin mRNA expression in rat cardiomyocytes. The maximum stimulatory effect occurred at 20ng/ml (p=0.007; fold-change vs. control=2.66).

mRNA expression of the chemerin receptor (Cmklr1) was decreased by treatment with TNF-α at 20ng/ml (p=0.031;fc vs.0.55). Dexamethasone induced a dose-dependent increase in chemerin mRNA expression with a maximum ef-fect at 100nm (p=0.002;fc vs.c=1.93) and the dexamethasone also induced a dose of 0.1-20nm with a maximum effect at 100nm (p=0.046;fc vs.c=2.87). Insulin induced a dose-dependent decrease of chemerin mRNA expression with maximum effect at 100nm (p=0.031;fc vs.c=2.06). The Cmklr1 mRNA levels were also decreased at dose-dependent re-sponse with a maximum effect at 100nm (p=0.018;fc vs.c=0.75). Western blot confirmed that results at protein level.A delayed weaning is able to decrease car-diac chemerin mRNA levels, independently of diet (p=0.036). Chemerin mRNA levels were not regulated by diet or exercise in rats. However, exercise increased significantly the rat cardiac Cmklr1 mRNA levels both in atrium (p=0.004) and ventricle (p=0.0043).

Conclusions: Our data suggest that the novel adipokine chemerin is influenced by inflammatory signals and insulin at the cardiac level. The delay in weaning and exercise affects the chemerin and Cmklr1 levels respectively. This report provides the first clues about the potential role of this adipokine in an endocrine/paracrine system at the cardiomyocyte level and their potential involvement in inflammation and metabolism.

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Capillary endothelial fatty acid binding protein 4 and 5 are required for sufficient energy production in the heart
T. Iso, M. Kurabayashi. Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

Purpose: Endothelial cells (EC) of muscle-type continuous capillary act as func-tionally important interface between blood plasma and tissue fluid. Fatty acids (FA) are major FA substrate for energy production in the heart. FA binding proteins (FABP) are cytosolic FA chaperones that regulate cellular and systemic metabolism of lipids. Here, we hypothesize that capillary endothelial FABP4 and FABP5 play an important role in providing sufficient FA to the myocardium.

Methods and results: Immunohistochemistry revealed that both FABP4 and FABP5 were abundantly expressed in capillary ECs in heart and skeletal mus-cle. Uptake of a FA analogue, 125I-BMIPP was significantly reduced in these tissues in double-knockout mice for FABP4/5 (DKO) as compared with wild-type (WT) mice. Uptake of a glucose analogue, 18F-FDG, showed dramatic and com-parable inhibitory increase in glucose uptake in DKO hearts in vivo during fasting.

These findings strongly suggest that FABP4/5 function as endothelial FA carriers between microvessels and interstitial fluid in trans-endothelial FA transport. We next explored molecular mechanisms underlying dramatic change of metabolism in DKO hearts. Expression of transcripts for mitochondrial oxidative catalytic machinery was reduced during fasting while those on glycolytic pathway were not altered in DKO hearts. Of note, metabolome analysis revealed that phosphocrea-tine (PCr), reserve energy and ADP levels were significantly lower in DKO hearts while ATP content was kept at a normal level, suggesting reduction in ATP synthesis rate which is replenished by PCr and ADP. Protein expression of glucose transporter Glu4 and phosphorylated form of PKCz (an enzyme to produce fruc-tose 2,6-bisphosphate, a potent activator for glycolysis) were increased in DKO hearts whereas phosphorylation of insulin receptor-b and Akt was comparable between WT and DKO hearts during fasting. Serum level of insulin was comparably decreased during fasting. These findings suggest that an increase in glucose utilization in DKO hearts during fasting is insulin-independent, and at least partly attributed to post-translational and allosteric regulation of the key proteins regulating glu-cose uptake and glycolysis, probably in response to shortage of ATP production by impaired FA uptake.

Conclusions: We conclude that capillary endothelial FABP4/5 is required for the uptake of circulating FA to supply sufficient energy substrate to the my-cardium. These findings identify FABP4/5 as promising targets for controlling the metabolism of energy substrates in the heart.

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Cardiac metabolism during atrial fibrillation is characterized by increased lipid accumulation and glycogen synthesis
M. Lenski, G. Schleider, L. Adrian, M. Kohlhass, C. Maack, M. Boehm, U. Laufs. Saarland University Hospital, Department of Internal Medicine III, Cardiology, Homburg, Germany

Background: The glucose and fatty acid (FA) metabolism in atrial fibrillation (AF) is largely unknown. However, metabolic changes may contribute to atrial myocardial remodelling during AF.

Methods and results: Tissue samples of the left atrium (LA) of patients with AF and sinus rhythm were compared. Western blot (WB) analyses showed an elevated expression of α2-subunit of the AMP-activated protein kinase (AMPK) (16%±18%). Expression of the catalytic subunit of protein phosphatase 2 A increased to 140±19%. As a result, phosphorylation of acetylCoA carboxylase (ACC), that regulates FA oxidation, was reduced to 68±11%. Immunofluorescence staining and WB analyses showed an increased expression of adipose differentiation-related protein, a marker for lipid accumulation, to 281±58% in AF. This was accompanied by decreased membrane expression of

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