The treatment had no hemodynamic effects in non-diabetic control animals. Diabetes+cinaciguat group compared to control (44.2 ± 3.3 vs. 83.0 ± 5.5mmHg; p < 0.05) and a marked diastolic dysfunction (time constant of LV pressure decay, Tau: 17.3 ± 0.8 vs. 10.3 ± 0.3ms), which was significantly improved by cinaciguat (PRSW: 66.8 ± 3.6mmHg, Tau: 14.9 ± 0.6ms in the diabetes+cinaciguat group). The treatment had no hemodynamic effects in non-diabetic control animals. diabetes mellitus

Methods: In male Sprague-Dawley rats diabetes was induced by a single ip injection of streptozotocin (60mg/kg). cinaciguat (10mg/kg/d) was applied orally for 8 weeks. Rats of the control groups received vehicle for the same time. After the treatment left ventricular (LV) pressure-volume relations were measured by using a micropipill Millar pressure-volume conductance catheter, and indexes of contractility (e.g. preload recruitable stroke work (PRSW)) were calculated. Blood plasma and myocardial tissue samples were collected for determination of cGMP-levels and immunohistochemical analysis, respectively. Myocardial gene expression analysis has been performed by quantitative real-time polymerase chain reaction (qRT-PCR).

Results: When compared to the non-diabetic controls, diabetic rats showed impaired left ventricular contractility (PRSW: 49.5 ± 3.3 vs. 83.0 ± 5.5mmHg; p < 0.05) and a marked diastolic dysfunction (time constant of LV pressure decay, Tau: 17.3 ± 0.8 vs. 10.3 ± 0.3ms), which was significantly improved by cinaciguat (PRSW: 66.8 ± 3.6mmHg, Tau: 14.9 ± 0.6ms in the diabetes+cinaciguat group). The treatment had no hemodynamic effects in non-diabetic control animals. Diabetes mellitus

Conclusion: Glucagon-like peptide-1 receptor activation ameliorates cardiac steatosis and reverses pathological remodelling by quality control of mitochondria via cAMP/PKA axis

Methods: Male KK/Ay mice (16-week-old) were allocated into exendin-4 (24 mmole/kg/day, 40 days) and vehicle group (KK-v). Male C57BL/6 mice were fed with high fat diet for 3 months and subjected to exendin-4 treatment at the age of 16 week old (DIO-ex4 and DIO). KK-ex4 exhibited decline in heart weight (-16.5% vs KK-v) without body weight loss. Oil-red-O staining revealed that KK-ex4 and DIO-ex4 reduced cardiac steatosis. Echo-cardiography revealed that systolic function of DIO was suppressed (-13.8% vs control), which was restored in DIO-ex4 with reduced LVSW (11.1% vs DIO-v) and IVSd (30.0% vs DIO-v). Myocardial fibrosis and tissue oxidative stress detected by DHE staining were reduced in KK-ex4 and DIO-ex4 (0.45±0.10 fold and 0.68±0.10 fold, respectively). Transmission electron microscopy revealed restoration of irregular alignment and increase in number of mitochondria with normal cristae in KK-ex4 and DIO-ex4. Mitochondria-specific dyes (MitoTracker Red) revealed decline in oxidative activity of cardiac mitochondria both in KK-ex4 and DIO-ex4. The levels of myocardial PINK/Parkin, the surrogate indicators for damaged mitochondria, were reduced both in KK-ex4 and DIO-ex4.

Conclusion: Cx43 hemichannels of the inner mitochondrial membrane are constitutively active in heart failure

Methods: We aimed to directly prove the presence of human miR-Cx43 hemi and to evaluate channel characteristics in failing versus non-failing myocardium. Furthermore we combined heart failure with ischemia-reperfusion injury in a mouse model. We used direct single-channel recordings of cardiac mitochondria to possibly identify a functional link between miR-Cx43 hemi and susceptibility to ischemic injury in murine and human heart failure.

Results: We identified single-channel currents, which were clearly distinct from mitoATP channels, inhibited by the Cx43 mimetic peptide 43GAP27 which suppressed cardioplegic injury and single-channel conductance. Single-channel properties thus supported the notion that we were recording mitochondrial Cx43 channels. Basal miR-Cx43 hemi activity was increased in both human and murine heart failure. A pharmacological preconditioning with diazoxide stimulated single-channels of failing and non-failing hearts to a similar maximal activity. Despite a reduced content and dephosphorylation of total Cx43 in failing hearts, mitochondrial Cx43 was increased and hyperphosphorylated.

Conclusion: For the first time we directly recorded human miR-Cx43 hemichannels which were inhibited by 43GAP27. Our results indicate endogenous protective adaptation mediated via enhanced basal miR-Cx43 hemichannel activity through hyperphosphorylation of the mitochondrial Cx43 fraction in heart failure.

Expression and physiological role of the novel adipokine nesfatin-1 in cardiomcyocytes

Methods: Real-time PCR was used to determine nesfatin-1 mRNA levels in cultured neonatal cardiomcyocytes of Sprague Dawley rats treated with TNF-α, dexamethasone and insulin. In heart tissue of rats fed with high fat diet for 16 weeks, we used real-time PCR to determine nesfatin-1 cardiac mRNA levels and an ELISA to determine nesfatin-1 plasma levels. Cardiomcyocytes were treated with nesfatin-1 and confocal microscopy was used to study the glucose transporter Glut-4 mobilization. Finally, western blot was used to identify possible transduc- tional signalling molecules (EκBα, AMPK and AKT) after nesfatin-1 treatment in cardiomcyocytes.

Results: Cardiomcyocytes treated with 0.1-20 ng/ml TNF-α for 6-48 h induces an increase of nesfatin-1 mRNA levels with a maximum stimulatory effect at 20 ng/ml for 24 h (p=0.0159; Fold-Change (FC)=1.16, n=5). Treatment with 0.1-100 nM dexamethasone for 6-48 h also increases nesfatin-1 mRNA levels with a maximum stimulatory effect at 100 nM for 24 h (p=0.0079; FC=2.457, n=5).

Figure 1. Typical mitochondria images by TEM

Figure 2. The soluble guanylate cyclase activator cinaciguat inhibits cardiac dysfunction in diabetic diabetes mellitus

Methods: Patients with diabetes mellitus exhibit cardiovascular dysfunction along with increased oxidative stress and decreased nitric oxide – cyclic guanosine monophosphate (cGMP) signalling. It has been reported, that elevated intracellular cGMP-levels contribute to an effective cytoprotection against oxidative stress. In this study we investigated the effects of cinaciguat, a newly developed soluble guanylate cyclase activator on myocardial dysfunction in type-1 diabetic rats.

Methods: We used direct single-channel recordings of cardiac mitochondria to postulate channel characteristics in failing versus non-failing myocardium. For the first time we directly recorded human miR-Cx43 hemichannels which were inhibited by 43GAP27. Our results indicate endogenous protective adaptation mediated via enhanced basal miR-Cx43 hemichannel activity through hyperphosphorylation of the mitochondrial Cx43 fraction in heart failure.
Conclusion: (r=-0.144, p=0.008) and KIDMED score (r=-0.111, p=0.041).

els (12.6 vs 20.5 mg/g, p=0.015). In the total population, ACR was associated to those with low KIDMED score exhibited higher systolic BP (117 vs 114 mmHg, p=0.043) and biochemical variables (fasting blood) were obtained according to standard methods. Design and Methods: A total of 365 adolescents 12-17 years of age [212 males, aged 13.9 years, office blood pressure (BP)=115/67 mmHg] that were included in the study evaluated the influence of AT1 receptor blocker losartan on insulin receptor signalling. Our data confirm based in data obtained in the general population that increasing the K intake may partially inhibit the hypertensive effect of high salt diets. This strategy seems to be more efficient in high salt consumers. Financial support – CNPq and FINEL.