AngII-induced inflammation were partly related to TLR4. Cotreatment of CFs with pioglitazone and AngII revealed no effect on AngII TypeI receptor (AT1), but downregulated AT1-dependent ERK1/2 phosphorylation. Furthermore, pioglitazone inhibited AngII-induced MCP-1 and TNF-α production and overexpression of TLR4, Myd88 and NF-κB; and increased nuclear-PPARγ production in CFs.
Conclusions: These results suggest that TLR4 is involved in the AngII-induced inflammatory responses in CFs, and pioglitzone provides its anti-inflammatory and antifibrotic effect which is partly depend on interfering with the TLR4-dependent signaling pathway (AT1/ERK1/2/TLR4/Myd88/NF-κB) to prevent the hypertension induced ventricle remodeling.

GW25-e0069

Ambulatory Blood Pressure Monitoring of Healthy Chinese Children Aged 5-12 Years

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Objectives: We studied the characteristics of ambulatory blood pressure (ABP) and their influence factors in healthy Chinese children.
Methods: Casual blood pressure (BP), ABP, body height, weight, body mass index (BMI), personal and familial medical histories were recorded in 338 Chinese children (aged 5-12 years). Data were treated by ABP database system and analyzed by SPSS 20.0 including correlations, regressions and conventional statistical methods.
Results: Means of 24-Hour SBP/DBP/PP (systolic BP/diastolic BP/pulse pressure) were 112.7±10.2/66.3±5.7/46.6±7.3 and 110.9±8.1/66.5±5.1/44.6±6.0 mmHg in normal weight 118 boys and 139 girls, and were 118.3±11.3/67.9±6.5/50.7±8.7 and 113.6±21.4/65.7±12.2/48.1±11.5 mmHg in overweight 46 boys and 35 girls, respectively. BMI, weight and gender were primary influencing factors on ABP-derived parameters. Overweight children had higher means ($P<.01$ or $<.05$) of systolic BP (SBP) and pulse pressure (PP), and higher hypertensive prevalence (35% vs. 15% for boys and 40% vs. 18% for girls) than normal weight children. Boys had higher ($P<.01$) means of PP (24-Hour /Daytime) than girls in normal weight children. Age related negatively with DBP and body height correlated with heart rate. Circadian variations of ABP (dipper pattern) were seen in most of children (76%). Familial histories of hypertension showed no influence on ABP.
Conclusions: BMI, weight and gender were the main influencing factors on ABP in Chinese children and our data provides basic information of ABP in Chinese children.

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Treatment of Myocardial Infarction by Transplantation of Adiponectin Gene-Modified Stromal Vascular Fraction cells from Adipose Tissue

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Objectives: The aim of this study was to investigate the effect of the human adiponectin (Hapm1) gene-modified stromal vascular fraction (SVF) cells (Hapm1-SVF) transplantation on the cardiac function and histological changes of heart tissue in rats with myocardial infarction.
Methods: Rats were divided into four groups (n=8) : sham-operated (sham), untreated myocardial infarction (MI), SVF treated (SVF), and HapM1-SVF (SVF carrying human adiponectin gene and labeled with EGFP) treated (HapM1-SVF) groups. The MI model was established by ligation of the left anterior descending coronary arteries. SVF were injected into the infracted border zone of MI rats. EF and FS were detected by echocardiography 4 weeks after the cells transplantation. LVSP and LVDP were measured by PowerLab biological signal analytical system. Vascular density was determined by immunohistochemical staining.
Results: It was shown that LVSP and LVDP were significantly increased in MI rats treated with SVF cells or HapM1 gene-modified SVF cells as compared with untreated MI rats, but still not reach the normal level [LVSP: sham (99.35±7.45) VS MI (72.83±5.37) VS SVF (77.85±7.82) VS Hapm1-SVF (84.23±8.65) mmHg, $P<0.05$]. EF and FS of rats in HapM1-SVF or SVF groups were significantly higher than that of MI rats, but still not reach the normal level (EF: sham (81.85±4.63%) VS MI (43.21±3.10%) VS SVF (64.93±4.13%) VS Hapm1-SVF (74.56±3.60%), $P<0.05$). Meanwhile, the density of vessels in HapM1-SVF group was higher than that in SVF or MI group, but still lower than that in sham group.
Conclusions: In summary, transplantation of SVF cells carrying hapM1 gene may stimulate recovery of cardiac function after myocardial infarction in rats.

GW25-e0435

Klotho Deficiency Causes Hypertension and Renal Damage and Its Mechanism

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Objectives: Klotho (KL) is a recently discovered aging-suppressing gene. Insertional mutation of KL gene resulted in a premature aging syndrome. Overexpression of KL gene extended the lifespan by 20% and rescued other aging disorders. Hypertension and kidney damage are common aging-related diseases. The purpose of this study is to assess if KL deficiency affects blood pressure (BP) and renal damage as well as the underlying mechanism.
Methods: One group of heterozygous mutant KL (KL (+/-)) mice and one group of wild type (WT) mice were used to measure BP continuously when they were from the age of 8 months to 13 months. Each strain of mice was further divided into 2 subgroups when the mice were at the age of 15 months, which received eplerenone treatment (6 mg/kg/day, IP) or an equal dose vehicle, respectively. BP was measured and urine was collected during treatment. At the end of the treatment for 3 weeks, the animals were sacrificed and blood was collected. Plasma aldosterone level was detected with an aldosterone ELISA kit. Kidney sections were used for periodic acid Schiff staining, Masson's trichrome staining and immunohistochemical staining (CD4, CD8, and CD68). Adrenal sections were used for immunohistochemical staining (klotho, CYP11B2). Plasma urea and creatinine level were detected with quantichromTM assay kits. Urinary albumin concentration was measured with a microalbuminuria ELISA kit. Western blotting was done to detect the expression of MR, SGK1, NCC, and ATP synthase β, TNF-α, MCP-1, IL-6 and osteopontin in kidney.
Results: The results demonstrated that the systolic BP was significantly and persistently elevated accompanied by aldosterone level increase and CYP11B2 (key enzyme of aldosterone synthesis) upregulation in KL (+/-) mice. Chronic treatment with eplerenone (aldosterone receptor blocker) decreased hypertension to the control level and prevented the upregulation of SGK1, NCC and ATP synthase β level in kidneys of KL (+/-) mice, suggesting that KL deficiency causes hypertension due to plasma aldosterone increase and the subsequent renal sodium retention through SGK1-NCC signaling. Moreover, significant renal structure damage (glomerulus collapse, tubule fibrosis) and function decline (plasma creatinine, urea and urine albumin increase) were observed in KL (+/-) mice. Further analysis indicated that several proinflammatory cytokines (TNFα, MCP-1, IL-6 and osteopontin) were upregulated and leucocyte (T cell and macrophage) infiltration were increased in kidneys of KL (+/-) mice. Eplerenone rescued KL deficiency-induced kidney damage and abolished the activated inflammatory process.
Conclusions: KL is essential to the maintenance of normal BP. KL deficiency caused hypertension and kidney damage *via* upregulating aldosterone level and consequently increasing inflammation and SGK1-NCC signaling in kidneys.

GW25-e1138

Cellular repressor of E1A-stimulated genes protects against angiotensin II-induced hypertension and vascular remodeling via p38MAPK-mediated regulation of the renin-angiotensin system

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Objectives: Cellular repressor of E1A-stimulated genes (CREG) has been proposed to be a new cardiovascular homeostasis regulator. We hypothesized that CREG is a negative regulator of angiotensin (Ang) II-mediated hypertension and vascular remodeling.
Methods: Ten-week-old male heterozygous CREG-deficient ($CREG^{+/-}$) mice and their littermate wild-type (WT) mice were implanted with osmotic minipumps containing saline, Ang II (1.5 mg/kg·d), or Ang II and recombinant human CREG (rhCREG; 15-300 μg/kg·d) protein for 14 days. Ang II-infused $CREG^{+/-}$ mice were then cotreated with p38 MAPK inhibitor, SB203580 (10 mg/kg·d), beginning 2 days before minipump implantation. Systolic blood pressure (SBP); extent of vascular remodeling; RNA and protein level of CREG, collagen type I/III, angiotensin-converting enzyme-2 (ACE2), angiotensin receptor type 1 (AT1R), Ets-1 and MAPK were evaluated. Primary vascular smooth muscle cell (VSMC) culture was performed to assess the mechanism of Ang II-induced CREG down-regulation, as well as CREG-mediated modulation of renin-angiotensin system.
Results: CREG levels are high in vascular media under basal conditions but rapidly decrease in response to Ang II. Ets-1 transcription factor expression is upregulated in Ang II-stimulated VSMCs. Chromatin immunoprecipitation analysis showed the interaction of endogenous and exogenous Ets-1 or glutathione S-transferase-tagged Ets-1, bearing only the DNA-binding domain with the authentic CREG promoter. Moreover, Ets-1 siRNA knockdown significantly reduced Ang II-induced repression of CREG expression, indicating Ets-1 mediates Ang II-induced down-regulation of CREG expression. Ang II infusion for 14 days resulted that levels of SBP, intima medial thickness and vascular remodeling of the aorta and mesenteric artery were significantly greater in $CREG^{+/-}$ mice compared with the WT controls. Vascular gene expression level of CREG was lower in Ang II-treated $CREG^{+/-}$ mice than in WT mice, suggesting that CREG deficiency aggravates Ang II-induced hypertension and vascular remodeling. However, daily treatment of Ang II-infused WT mice with rhCREG protein improved the above phenotypes. Ang II-induced vascular remodeling was inhibited by rhCREG protein in association with reduced plasma Ang II and increased plasma Ang 1-7 levels. Furthermore, rhCREG treatment inhibited Ang II-mediated up-regulation of AT1R expression and down-regulation of ACE2 expression by blocking p38MAPK activation. Finally, pharmacological blockade of p38MAPK with SB203580 abolished CREG deficiency mediated the aggravation of Ang II-induced hypertension and vascular remodeling.
Conclusions: Ets-1 mediates Ang II-induced down-regulation of CREG expression. Elevated Ang II induced hypertension and vascular remodeling, which were exacerbated by CREG deficiency, whereas rhCREG protein attenuated Ang II-induced hypertension and vascular remodeling through modulation of balance between