GW25-e1171
Analysis of long non-coding RNA expression patterns in cardiac fat pads of canine with atrial fibrillation
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Objectives: Long non-coding RNAs (lncRNAs) are indicated to be important orchestrators of gene regulatory networks. In this study, we aimed to characterize the lncRNA expression profiles in neural remodeling during atrial fibrillation (AF).

Methods: 6 adult beagle dogs of either sex were randomly divided into AF group (400 beats/min, right atrial pacing) and control group (without atrial pacing). After 4 weeks of tachypacing, the second-generation RNA sequencing was performed to examine the transcriptomes of lncRNAs in AF non-AF canine cardiac anterior right ventricle. The sequencing data were confirmed by quantitative real-time PCR (qRT-PCR). GO and KEGG pathway analyses were used to annotate the biological functions and pathways that the aberrantly expressed genes were involved in. Based on the sequence similarity, target genes of the lncRNA transcripts were predicted. Filtering pipelines were established to identify the candidate lncRNA transcripts.

Results: A sum of 61616 lncRNA transcripts was yielded by the high-throughput sequencing. Among them, 166 down-regulated and 410 up-regulated lncRNA transcripts with more than 2-fold change were identified, in which 45 transcripts were newly discovered in canine models of AF. 0 newly identified lncRNA transcripts were randomly selected and confirmed by qRT-PCR. Bioinformatic analysis showed that the aberrantly expressed genes were associated with neural growth, development, migration and neurodegenerative disorders. Additionally, based on differential expression levels, functions, and target genes, bioinformatic analysis and the tissue-specific analysis, we selected two new IncRNAs, TCONS_000323546 and TCONS_00026102, which might be involved in the process of neural remodeling by regulating their target genes at transcriptional level.

Conclusions: This study suggested that the dysregulated lncRNA transcripts might play a role in the initiation and development process of AF neural remodeling, which further provided potential therapeutic targets for prophylaxis and treatment of AF.

GW25-e1408
Hydrogen sulfide ameliorates High glucose-induced senescence by suppressing oxidative stress
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Objectives: In patients with diabetes, the level of hydrogen sulfide (H2S) is remarkably decreased. And it is demonstrated that endothelial senescence is accelerated under high glucose condition. The aim of this study is to investigate the effect of exogenous H2S on HUVEC senescence induced by high glucose.

Methods: Senescence model was established by treating HUVECs with 33 mMol/L glucose for 48 hours. Senescence was identified by β-galactosidase (SA-β-gal) staining and proliferation assay due to aberrant cell proliferation. PAI-1, SOD1 and NF-kB p65 was analyzed by western blot. MDA level was measured using a commercial kit.

Results: High glucose induced a senescence-like phenotype in HUVECs as shown by slower proliferation, more SA-β-gal positive cells and increased protein expression of PAI-1. In senescence model, the SOD1 expression was reduced dramatically, but NF-kB activity and MDA production was increased significantly. However, sodium hydrosulfide (NaHS, H2S donor, 100 μMol and 200 μMol/L) was able to promote cell proliferation, decrease the number of SA-β-gal positive cells and reduce PAI-1 expression. In the meantime, NaHS increased SOD1 expression, inhibited the activity of NF-kB p65 and decreased MDA production.

Conclusions: Exogenous hydrogen sulfide prevents HUVECs against high glucose-induced senescence by modulating oxidative stress and NF-kB p65 activity. Our results may indicate that hydrogen sulfide treatment would be helpful to improve endothelial function in diabetic patients. Further studies are needed to explore the value of hydrogen sulfide in clinical practice.

GW25-e2467
Expression of Neutrophil Gelatinase-associated Lipocalin in Hypotonic Contrast-induced Rat Model of Renal Injury and The Effect of N-acetylcysteine on NGAL
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Objectives: We built the rat model of contrast-induced nephropathy to observe kidney damage and the expression of neutrophil gelatinase-associated lipocalin (NGAL) in this situation. We also paid attention to the changes of NGAL level after the intervention of N-acetylcysteine (NAC) in order to know whether NAC could be used as an index for early diagnosis of contrast-induced nephropathy (CIN), and whether NAC could alleviate renal protective effects.

Methods: Adult male SD rats of clean grade (total number 80) were randomly divided into four groups: control group (CON), contrast-induced nephropathy group (CIN), N-acetylcysteine group (NAC), and NAC plus CIN group (NAC+CIN). We collected blood samples and renal tissue of each group at the time point of 2h, 12h, 24h, 48h, and 72h after modeling (4 rats per time point of each group). Serum creatinine (Scr) values were measured by an automatic biochemical analyzer. Concentration of NGAL in serum was evaluated by Enzyme linked immunosorbent assay (ELISA) by using commercial kit. Immunohistochemistry and Western Blotting method is used to determine the expression of NGAL in renal tissue. HE-stained sections of rat kidneys were used to assess the damage degree of kidney. At the same time, renal oxidative stress was analyzed by MDA and T-SOD value.

Results: (1) Scr values: 2h, 12h and 24h after modeling, there showed no difference between the Scr values of CIN and CON group (P>0.05), 48h or 72h after modeling, Scr value was significantly increased in CIN group than in CON group or NAC+CIN group (P<0.05). There’s no significantly difference between the Scr value of NAC+CIN group and CON group 48h after modeling (P>0.05), but difference appeared at the time point of 72h (P<0.05). (2) Kidney damage assessment of HE staining: 12h, 24h, 48h, 72h after modeling, different degrees of tubular injury occurred in CIN group, with or without epithelial cell brush border shedding, vacuolar degeneration, cell loss and regeneration, even part of tubular structural damage. At the time point of 12h, 24h, 48h or 72h, CIN group significantly showed more damage than CON group (P<0.05), and the damage scores of NAC+CIN group are higher than CON group too (P<0.05), but NAC+CIN group showed less damage than CIN group at the same time (P<0.05). Functional analysis: The main effect of contrast agent was statistically significant (F=64.128, P<0.01). The interaction of contrast agents with NAC was statistically significant. (3) Serum NGAL level: 2h, 12h, 24h, 48h or 72h after modeling, serum NGAL level of CIN group is obviously higher than CON group (P<0.05), but that of NAC+CIN group is lower than CIN group (P<0.05). There was no difference between the serum NGAL levels of NAC+CIN group and CON group 2h after modeling (P>0.05). (4) Immunohistochemistry: 12h, 24h, 48h or 72h after modeling, NGAL expression of CIN group was significantly increased than CON group (P<0.05), (5) Western blot: 2h, 12h, 24h, 48h or 72h after modeling, the NGAL level in kidney of CIN group was significantly increased than CON group (P<0.05). (6) Correlation analysis of tubular injury score and serum NGAL values shows that there’s a positive correlation between them.

Conclusions: (1) The changes of kidney function and serum appear early in CIN rat model, and there’s a positive correlation between tubular injury score and serum NGAL values. (2) NAC can reduce the renal tubular epithelial cell injury in CIN model, this effect may be produced through oxidative stress pathways.

GW25-e3118
Lin28A Protects Against Cardiac Ischemia/Reperfusion Injury in Diabetic Mouse through the Insulin -PI3K-mTOR pathway
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Objectives: The insulin-PI3K-mTOR pathway exhibits a variety of cardiovascular activities including protection against IR injury. Lin28A enhanced glucose uptake and insulin-sensitivity via insulin-PI3K-mTOR signaling pathway. However, the role of lin28a on experimental cardiac IR injury in diabetic mice are not well understood. The aims of the present study were to (1) determine whether lin28a protects diabetic mice from cardiac IR injury and (2) identify whether the underlying mechanisms of lin28a is associated with the insulin-PI3K-mTOR dependent pathway.

Methods: Diabetic mice underwent 30 minutes of ischemia followed by 3h of reperfusion. Animals were randomized to be treated with lentivirus carrying lin28a siRNA (siLin28a) or control virus (siControl), lin28a cDNA (Lin28a) or control virus (Mock) 4 weeks of tachypacing, the second-generation RNA sequencing was performed to examine the transcriptomes of lncRNAs in AF non-AF canine anterior right ventricle. GO and KEGG pathway analyses were used to annotate the biological functions and pathways that the aberrantly expressed genes were involved in. Based on differential expression levels, functions and target genes of the lncRNA transcripts were predicted. Filtering pipelines were established to identify the candidate lncRNA transcripts.

Results: A sum of 61616 lncRNA transcripts was yielded by the high-throughput sequencing. Among them, 166 down-regulated and 410 up-regulated lncRNA transcripts with more than 2-fold change were identified, in which 45 transcripts were newly discovered in canine models of AF. 0 newly identified lncRNA transcripts were randomly selected and confirmed by qRT-PCR. Bioinformatic analysis showed that the aberrantly expressed genes were associated with neural growth, development, migration and neurodegenerative disorders. Additionally, based on differential expression levels, functions, and target genes, bioinformatic analysis and the tissue-specific analysis, we selected two new IncRNAs, TCONS_000323546 and TCONS_00026102, which might be involved in the process of neural remodeling by regulating their target genes at transcriptional level.

Conclusions: This study suggests that the dysregulated lncRNA transcripts might play a role in the initiation and development process of AF neural remodeling, which further provided potential therapeutic targets for prophylaxis and treatment of AF.

GW25-e3219
Urotensin II induces endothelial-mesenchymal transition of cardiac microvascular endothelial cells via Smad2/3 activation
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Objectives: Cardiac fibrosis is associated with the emergence of fibroblasts origin-ating from endothelial cells through endothelial-mesenchymal transition (EndMT). The aim of the study was to explore the effect of U11 on EndMT and its possible mechanisms.

Methods: Growth-arrested cardiac microvascular endothelial cells from neonatal rats were incubated in serum-free medium with U11 (10^{-6}mol/l) and its receptor antagonist SBT710411 (10^{-7}mol/l). To investigate the roles of Smad2, Smad3 in EndMT induced by U11, a small interfering RNA (smad2 siRNA or smad3 siRNA) were transfected into the cells. The phosphorylated Smad2/3 protein levels, 2-smooth muscle-actin (2-SMA) and VE-cadherin induced by U11 were evaluated by western blot. The CD31 were evaluated by flow cytometry.

Results: U11 induced 2- SMA expression in a dose-dependent manner, with maximal effect at a concentration of 10^{-6}mol/l (23.4%). It decreased VE-cadherin expression in a dose-dependent manner, with maximal effect at a concentration of 10^{-6}mol/l (91.3%). U11 induced significantly reduced expression of CD31. In addition, U11 promoted Smad2/3 phosphorylation in a time-dependent manner, with maximal effect at 24h (811.6%). The effect was significantly inhibited by treatment with the UT inhibitor SB710411 (10^{-7}mol/l). Furthermore, Knockdown of Smad2 and Smad3 expression with siRNA significantly reversed the effect of U11.

Conclusions: Our data show for the first time that U11 stimulates endothelial-mesenchymal transition, which is mediated partly by the activation of the Smad2/3 signal pathways.

GW25-e3239

Geniposide Protects against Pressure Overload-Induced Cardiac Remodeling via 5'-Adenosine Monophosphate-Activated Protein Kinase-2

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Objectives: Cardiac remodeling featured as left ventricular dilatation, fibrosis, and increased wall thickness opposes the effects of angiotensin II receptor blockade to heart failure. Geniposide (GE) is widely presented in traditional herbs possessed of anti-tumor effect. Whether GE protects pressure overload-induced remodeling has not been identified yet.

Methods: The mice were orally treated with GE (25-50mg/kg) for 7 weeks beginning the first time that UII stimulates endothelial-mesenchymal transition,, which is mediated partly by the activation of the Smad2/3 signaling pathways.

GW25-e3348

Atrial Fibrillation Electrical Remodelling via Ablation of the Epicardial Neural Networks and Suprathreshold Stimulation of Vagosympathetic Nerve

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Objectives: Vagosympathetic nerve stimulation and epicardial neural networks are important participants in atrial electrical remodelling (AER). Elucidation of the changes in the electrophysiological indicators of the atrial and pulmonary veins caused by stimulation of epicardial neural networks (ENW) may provide a theoretical basis for the clinical treatment of atrial fibrillation (AF).

Methods: A total of 13 beagle dogs were randomly divided into two groups: the control group (n=6), which was treated with a simple rapid atrial pacing (RAP) for 6 minutes; the experimental group (n=7), which was treated with RAP+vasoactive (Vasopressin, VAS) stimulation of VNS for 6 minutes. Both groups were treated with epidural ganglia plexus (GP) ablation after 6 h. The monophasic action potential (MAP), various parts of the effective refractory period (ERP) and AF induction rate were measured and recorded at 15 min.

Results: With the extension of the pacing record time, the atrial MAP and ERP of the two groups shortened and AF induction rate increased in various sites (P <0.05). Compared with control group, MAP and ERP shortened significantly, while atrial fibrillation inducing rate increased significantly at baseline and 1 h, 3 h, and 6 h after pacing in experimental group (P <0.05). Following GP ablation, the atrial MAP, ERP and AF induction rate were not different from baseline levels (P >0.05).

Conclusions: Vagus nerve threshold stimulation exacerbated the deterioration of electrophysiological remodelling, whereas the epicardial neural network ablation blocked or reversed the AER.