CRM1 inhibitor. ATP levels were detected by enhanced ATP kits, and enzymes in fatty acid oxidation were detected by qPCR.

RESULTS The levels of ATP were increased by CRM1 inhibitor. ($P<0.05$), and CPT2, acadvl were also increased.

CONCLUSIONS Increased nuclear NT-PGC-1α may increase fatty acid oxidation to supply more ATP, which can provide a novel target in heart failure therapy.

GW27-e0446

Microarray Analysis of Differential Gene Expression Profile between Human Fetal and Adult Heart

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OBJECTIVES Although many changes have been discovered during heart maturation, the genetic mechanisms involved in the changes between immature and mature myocardium have only been partially elucidated. Here, gene expression profile changed between the human fetal and adult heart was characterized.

METHODS A Human Microarray was applied to define the gene expression signatures of the fetal (13 - 17 weeks of gestation, n = 4) and adult hearts (30 - 40 years old, n = 4). Gene ontology analyses, pathway analyses, gene set enrichment analyses and signal transduction network were performed to predict the function of the differentially expressed genes. Ten mRNAs were confirmed by quantificational real-time polymerase chain reaction(qRT-PCR).

RESULTS 5547 mRNAs were found to be significantly differentially expressed. "Cell cycle" was the most enriched pathway in the down-regulated genes. EFGR, IGF1R and ITGB1 play a central role in the regulation of heart development. EGFR, IGF1R and FGFR2 were the core genes regulating cardiac cell proliferation. The qRT-PCR results were concordant with the microarray data.

CONCLUSIONS Our data identified the transcriptional regulation of heart development in the second trimester and the potential regulators that play a prominent role in the regulation of heart development and cardiac cells proliferation.

GW27-e0448

Age-related expression of calcium channels and related proteins in Ventricular Myocyte during embryonic heart development

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OBJECTIVES To explore the age-related expression of calcium channels, Ca2+ handler proteins, hormone receptors and transcription factors in Ventricular Myocyte during mouse embryonic heart development.

METHODS By using real-time PCR assays to investigate the dynamic changes in the expression of calcium channels and related proteins in mouse ventricular myocytes from embryonic 12 days, embryonic 15 days, embryonic 18 days, postnatal 1 day and adulthood.

RESULTS During mouse embryonic heart development, the expression of most proteins was increased along with heart development. On the one hand, the expression of several proteins, such as Cav1.2 (α1C), Cav1.3 (α1D), Cav3.2 (α1H), IP3R1, IP3R2, CaMKIId, Nkx2.5, GATA4 and Tbx5, was highest in embryonic 15 days. Expression of most proteins decreased around embryonic 18 days, postnatal 1 days and adulthood. However, Cav1.2 still maintained high expression in adulthood. On the other hand, the expression of proteins, including Cav3.1 (α1G), RyR2, Agtr1a and Agtr1b, increased during embryonic heart development, peaked at embryonic 18 days, and then Cav3.1 decreased sharply around postnatal 1 day and adulthood, but RyR2, Agtr1a and Agtr1b still have a high expression.

CONCLUSIONS The expression of calcium channels, ca2+ handler proteins, hormone receptors and transcription factors in Ventricular Myocyte showed an age-related changes during mouse embryonic heart development. Most of these proteins expressed highest in embryonic 15 days and decreased subsequently.

GW27-e0449

CircRNA_000203 enhances expressions of fibrosis-associated genes through blocking miR-26b in cardiac fibroblasts

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OBJECTIVES Circular RNAs (circRNAs) participate in regulating gene expression in diverse biological and pathological processes. The present study aimed to investigate the mechanism underlying the modulation of circRNA_000203 on expressions of fibrosis-associated genes in cardiac fibroblasts.

METHODS Masson trichrome staining was performed on the myocardium of the diabetic db/db mice and the nondiabetic db/m control mice. CircRNAs expression profile in the diabetic myocardium was detected by circRNAs microarray, followed with the identification of circRNA_000203 expression by quantitative reverse transcription PCR (RT-qPCR). Dual luciferase reporter assay was used to confirm the target genes of miR-26b. Expressions of Col1a2, Col3a1and other concerned genes were determined by RT-qPCR and western-blot assay, respectively.

RESULTS CircRNA_000203 was shown upregulated in the diabetic mouse myocardium and TGF-β1-induced mouse cardiac fibroblasts. Enforced-expression of circRNA_000203 could increase expressions of Col1a2, Col3a1 and α-SMA in mouse cardiac fibroblast. Bioinformatics analysis indicated that microRNA-26b (miR-26b) has two potential binding sites in circRNA_000203, Col1a2 and CTGF were candidate targets of miR-26b. Dual luciferase reporter assay revealed that miR-26b interacted with 3′UTRs of Col1a2 and CTGF, and circ_000203 could block the interactions of miR-26b and 3′UTRs of Col1a2 and CTGF. Transfection of miR-26b could post-transcriptionaly inhibit expressions of Col1a2 and CTGF, accompanied with the suppressions of Col3a1 and α-SMA in cardiac fibroblasts. Additionally, over-expression of circRNA_000203 could eliminate the anti-fibrosis effect of miR-26b in cardiac fibroblasts.

CONCLUSIONS Suppression of the function of miR-26b contributes to the pro-fibrosis effect of circRNA_000203 in cardiac fibroblasts.

GW27-e0470

Mutations in SCAP and AGXT2 Revealed by Exome Sequencing in a Pedigree with Premature Myocardial Infarction

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OBJECTIVES To investigate the causative genes of myocardial infarction (MI) in a pedigree with multiple members with premature myocardial infarction (PMI) by whole-exome sequencing and functional verification.

METHODS PMI was defined by MI diagnosed before the age of 50 for men and 60 for women. Peripheral blood of all the family members (n=17) was obtained under informed consent for DNA extraction. Whole-exome sequencing was performed on 8 individuals from a PMI pedigree with two siblings diagnosed with MI before the age of 45 as well as their uncle at the age of 53. Bioinformatics analysis served as a tool for causative gene screening. Another 100 PMI patients were also enrolled for population validation of the potential causative genes. Finally, the potential causative genes were introduced into corresponding model cell lines by CRISPR-Cas9 technology, after which the functional consequences of the mutations were evaluated by western-blot and enzyme-linked immune-sorbent assay (Elisa).

RESULTS Upon exome-sequencing and subsequent Bioinformatics analysis, two variants in SCAP (c.3035C>T, p.Ala1012Val) and AGXT2 (c.1103C>T, p.Ala338Val) were identified as potential causative mutation for PMI. It was noteworthy that only patients that meet the diagnosis of PMI (n=2) harbored two variants all together, while other MI patients or members with no MI carried only one or no above variants.

We then screened the two genes in an independent population with PMI. Another variants was identified on SCAP (c.1403 T>C, p.Val468Ala), which was absent in 28, 000 east-Asian population. However, no potential causative mutation on AGXT2 was found in the present population.