**miRNA-449 PROMOTE DIABETIC CARDIAC FIBROSIS BY THE SMAD3 PATHWAY**

**H. Liu**

Qinghai University Medical College, Xining, China

**Objective:** Study role of miRNA-449 in diabetic cardiac fibrosis.

**Method:** Heart function of 16-week-old db/db mice and db/mice in control group was evaluated with B ultrasound. miRNA expression profile of myocardium was detected by biochip. Assay fibrosis related genes and mature miRNA expression with real-time PCR. Fibrosis related protein and Smad3 pathway protein were detected by Western blot. Proliferation of myocardial fibroblasts tested with flow cytometer. Assay binding ability of miRNA-449 to 3’UTR of KCNN3 by dual-luciferase report assay system.

**Results:** Left ventricular systolic and diastolic was dysfunction and abnormal with eject fraction in 16-week-old db/db mice. Phosphorylation of Smad3 and fibrosis related genes expression in diabetic myocardium was increased and miRNA expression profile was disturbance. Expression of miRNA-208b in myocardium of db/db mice increased obviously. miRNA-449 activate Smad3 pathway and increased expression in myocardium and cardiac fibroblasts by AnglI,TGF-131 and glucose/glucose oxidase(G/GO) and also up-regulated expression of Collal,α—SMA and CTGF in myocardium with a dose-dependent manner. Expression of miRNA-449 was decreased after Smad3 pathway inhibited and expression of Coilal, α-SMA and CTGF were down-regulated after miRNA-449 inhibited. miRNA-449 inhibit expression of KCNN3 at the level of post-transcriptional. Expression of fibrosis related genes in myocardium was up-regulated after inhibit KCNN3.

**Conclusion:** miRNA-449 is high expression in diabetic myocardium and promote fibrosis related genes such as Coilal,α-SMA and CTGF expression which induced with KCNN3 and Smad3 pathway and promote diabetic cardiac fibrosis.