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INDUCED CARDIAC MYOCYTES APOPTOSIS IN VITRO BY MICRORNA-122 OVER EXPRESSION

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Objective The role of microRNA-122 (miR122) in myocardial cells is still unknown. Thus we investigated the involvement of miRNAs in the knockout Pax8 mice and study the function of miR122 during cardiac development.

Methods The knockout Pax-8 mice model was established and the heart morphology of Pax-8 KO-/-, and Pax-8 KO+/- mice were detected. The total RNA of Pax-8 KO-/-, and Pax-8 KO+/- mice were extracted. MicroRNA microarray was used to investigate the differentially expressed microRNAs between Pax-8 KO-/-, and Pax-8 KO+/- mice, and the discovered microRNAs were further confirmed by real-time quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR). Primary cultured H9C2 (2-1) myocytes were transfected with extraneous miR-122 mimics to up-regulate the level of miR-122 expression and the transfection was confirmed by qRT-PCR. Myocytes apoptosis was determined by means of CCK-8, caspase-3 and flow cytometry.

Results Ventricular septum defect in Pax-8-/- mice, and many apoptotic cells in left ventricular wall and interventricular septum in Pax-8 KO-/- mice were found. Differential expression profiles of miRNAs in Pax-8 KO-/- mice and Pax-8 KO+/- mice showed 10 microRNAs expressed differently between the two kinds of mice. miR-122 was up-regulated by 1.92 folds in Pax-8 KO-/- mice . Up-regulating the Level of miR-122 expression in primary cultured H9C2 (2-1) myocytes promoted cardiac myocytes apoptosis and inhibited myocytes proliferation. Taken together, these studies demonstrate that miR-122 is a critical regulator of heart development and ventricular septum defect pathogenesis.