37. Angiotensin II Reduces the Expression of Cx43 and Inhibits the c-SRC /MAPK/ERK Pathway Via Cx43 in Cardiomyocytes

Xin Fan, XinRong Chen, RunMin Sun, WenJuan Wang, Xu Zhao, ChengKun Kou, QiongYing Wang, Jing Yu, Lanzhou University Second Hospital, Lanzhou, Gansu Province, China

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Background: Hypertension is associated with abnormal renin angiotensin system (RAS). Angiotensin II (AngII), an important substance in RAS, is closely related to cardiomyocyte injury. Connexin43 (Cx43), a key structural protein in cardiomyocyte membrane, takes part in signal transduction and substance transport. Cx43 may cause extracellular interstitial fibrosis.It is known that Cx43 increases collagen I in heart tissue by regulating nuclear factor kappa B and Mechanistic metalloproteinase.However, the relationship between Ang II and Cx43 has been controversial,and how Ang II affects Cx43-related pathway is unclear. Otherwise, the activation and inhibition of the c-SRC /MAPK/ERK pathway may is related to Cx43, but the fact which is the forward is not sure.

Objective: The purpose of this study is to explore whether Ang II affects the expression of Cx43 and inhibits c-Src /MAPK/ERK pathway via Cx43.

Methods: First,we given rat cardiomyocytes (H9C2 cells) different concentrations of Ang II (10-5M,10-6M and 10-7M， for 48h), and establish Ang II groups. There is a contral group, which was given normal culture without Ang II. Second,we given H9C2 cells the Gap26,which is the inhibition of Cx43.Proteins of Cx43 and c-SRC /MAPK/ERK pathway from all groups were detected by Western Blot, and mRNA of these proteins were detected by PCR. SPSS was used for statistical analysis to compare the difference between all the groups.

Results: First, compared with the control group, protein of Cx43, c-SRC, ERK2 and ERK1 were significantly decreased in Ang II group, and when the concentration of Ang II was 10-5M, these proteins were the least. mRNA of Cx43, ERK2 and ERK1 also were cut down after giving Ang II (only 10-5M).Second, the Gap26-intervention group had the lower expression protein and mRNA of Cx43, c-SRC, ERK2 and ERK1.

Conclusion: We proved that Angiotensin II can reduce the expression of Cx43 and inhibit c-SRC /MAPK/ERK pathway via Cx43 in cardiomyocytes.Based on the role of Cx43 and c-Src /MAPK/ERK pathway, hypertesion may injury the cardiomyocytes via RAS and these pathways.

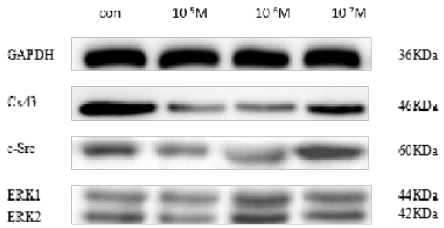

Figure1 The expression of Cx43, C-Src, ERK1 and ERK2 proteins affer giving different concentrations of AngII

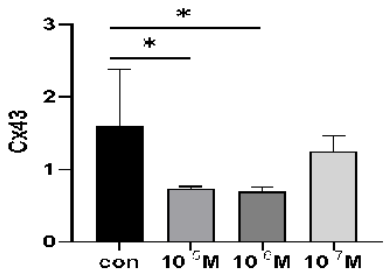

Figure2 The expression of Cx43 affer giving different concentrations of AngII

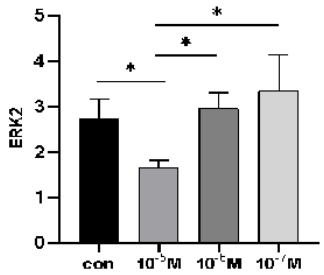

Figure5 The expression of ERK2 affer giving different concentrations of AngII

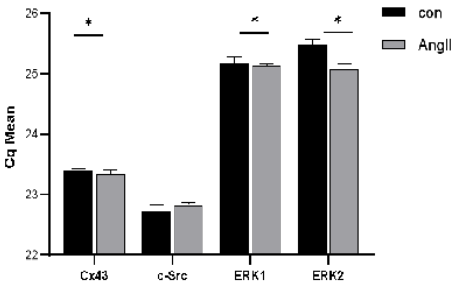

Figure6: The mRNA expression of Cx43, C-SRC, ERK1 and ERK2 after giving AngII

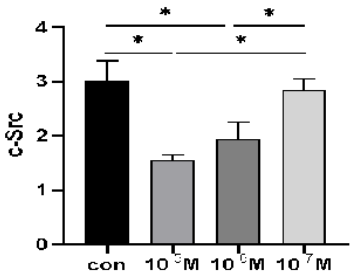

Figure3 The expression of c-Src affer giving different concentrations of AngII

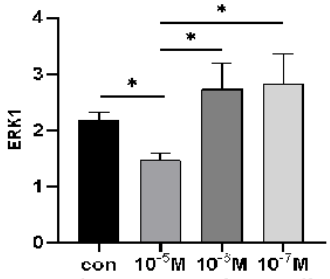

Figure4 The expression of ERK1 affer giving different concentrations of AngII

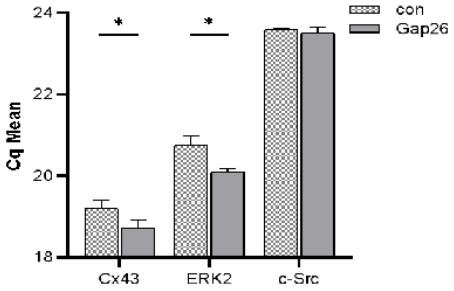

Figure7: The mRNA expression of Cx43, C-SRC, and ERK2 after giving Gap26

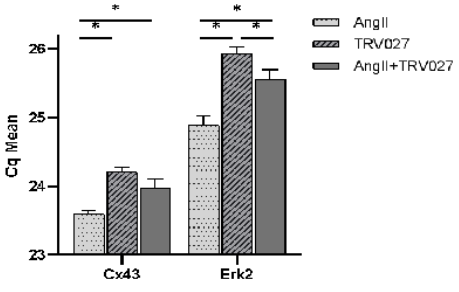

Figure8: The mRNA expression of Cx43, and ERK2 after giving Gap26

Clinical Implications: My study will help enable cardiovascular clinicians to explore the relationship between RAS and Cx43 and cardiomyocytes injury.