0180
Trps1 Promotes Tubular Cell Proliferation After Renal Ischemia-Reperfusion Injury Through Transactivation of Notch2

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Background: Trichorhinophalangeal 1 (Trps1) is essential for epithelial cell morphogenesis during kidney development. But its role in acute kidney injury induced by ischemia/reperfusion (I/R) remains unclear.

Methods: The rat models of renal I/R injury were established by clamping bilateral renal arteries for 45 min (moderate I/R) or for 60 min (severe I/R) and reperfusion. The renal tubule epithelial NRK-52E cells were cultured under hypoxic conditions for 4 h to induce hypoxic injury, followed by reoxygenation (H/R). Trps1-siRNA or Trps1-overexpression vectors were transferred by ultrasound-microbubble-mediated gene transfer system. The changes of gene expression were analyzed by real-time PCR and Western blotting. Promoter activities of transcription factors were estimated by dual luciferase reporter gene assay.

Results: Knockdown of Trps1 significantly delayed renal repair in moderate I/R model as evidenced by higher serum creatinine levels and more severe morphological injury compared with wild-type rat (P < 0.05), whereas overexpression of Trps1 significantly accelerated renal repair after severe I/R injury. Knockdown of Trps1 decreased the proportion of IDU positive cells in rat kidneys with I/R injury and the level of PCNA in NRK-52E cells after H/R, and vice versa. Furthermore, mRNA level of Notch2 was decreased by 58% and the protein levels of Notch2 and its downstream effector molecule Hes1 were decreased by about 43–67% in Trps1-knockdown rat at 3 day after reperfusion. The dual luciferase analysis demonstrated that Trps1 directly activated Notch2 transcription. And knockdown of Notch2 significantly inhibited Trps1-induced tubular cells proliferation in vitro.

Conclusion: Trps1 regulates tubular cells proliferation through Notch2 and promotes kidney repair after I/R injury. Trps1 may serve as a potential therapeutic target for renal repair following I/R injury.

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0184
Clinical Risk Model to Predict Acute Kidney Injury After Cardiac Surgery in Chinese Patients

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Objective: To establish and validate a risk model to predict AKI after cardiac surgery (AKICS) based in Chinese patients.

Methods: 7233 patients who underwent cardiac surgery (CABG, OPCAB, valve surgery or CABG with/without valve surgery) in the Department of Cardiac Surgery in our centre between January 2010 and April 2013 were included. Logistic regression was used to analyze the incidence and preoperative risk factors of AKICS among 6081 patients, and a specific number of points were assigned to each risk factor according to the odds ratio (OR) observed, the other patients were set for validation, by means of Hosmer-Lemeshow goodness-of-fit test for the calibration and receiver operating characteristic (ROC) curves with area under the ROC curve (AUCROC) for the discrimination.

Results: The incidence of AKI and RRT after cardiac surgery in the derivation cohort were 23.8% (1446/6081) and 1.5% (93/6081) respectively. The mortality of derivation cohort was 2.8% (170/6081). According to the logistic regression: male (OR = 2.277), atrial fibrillation (OR = 1.766), preoperative kidney disease (without RRT) (OR = 3.904), preoperative coronary angiography (OR = 1.137), NYHA > 2 (OR = 1.457), were recognized as independent risk factors for AKI after cardiac surgery. The risk model was categorized to high risk cohort (total score ≥ 8) and low risk cohort (total score 9–12), the risk of AKI in the derivation cohort was 35.6% (low risk cohort) versus 83.4% (high risk cohort). The AUROC for AKICS of the validation cohort was 0.81, which meant a good discrimination, and Hosmer-Lemeshow goodness-of-fit test (χ2 = 10.13, p = 0.256) showed a proper calibration.

Conclusion: The risk model based upon chinese patients, with AKI being defined with the 2012 KDIGO AKI guideline is established and proper prediction value for AKICS is validated.

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0196
Effect of Body Mass Index on Acute Kidney Injury After Cardiac Surgery

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Objective: Among maintenance hemodialysis patients, the higher body mass index (BMI) was, the higher survival rate was. This study was to explore the relationship between BMI and incidence, mortality of AKI and AKI requiring RRT (AKI-RRT) after cardiac surgery.

Methods: Clinical data of patients undergoing cardiac surgery, which included demographic data of preoperative, intraoperative and postoperative were prospectively collected in Zhongshan hospital affiliated Fudan University from January 2009 to December 2013. According to BMI classification for Chinese: low weight group (BMI < 18.5 kg/m2), normal weight group (18.5 ≤ BMI < 24 kg/m2), overweight group (BMI < 28 kg/m2), obese group (BMI ≥ 28 kg/m2).

Results: A total of 8013 patients enrolled, including 4477 males and 3536 females with the mean age of 53.1 ± 14.0 years. The overall AKI incidence was 34.0% (n = 2723). The hospital mortality of AKI was 5.7% (n = 156). The incidence of AKI-RRT was 4.9% (n = 133). The morality of AKI-RRT was 58.6% (n = 78). The incidences of AKI in low weight group, normal weight group, overweight group, obese group were 27.8%, 31.4%, 35.7%, 45.0% (P < 0.001). The hospital mortality of AKI in four groups were 9.0%, 6.5%, 4.6%, 5.0%. There was no statistically significant difference (P = 0.426).

The hospital mortality of AKI-RRT in four groups were 62.5%, 61.3%, 51%, 75%, also no statistically significant difference (P = 0.062).
Acute Kidney Injury

Conclusion: BMI is an independent risk factor for AKI after cardiac surgery, the AKI incidence increased, as BMI gained. The hospital prognosis of AKI and AKI-RRT were optimum, when BMI was 24–28 kg/m².

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0201
Role of SIRT1 in Study of Renal Ischemia-Reperfusion Injury and Its Effect on NF-κBp65-PGC-1α Signal Pathway In Mice
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Objective: To investigate the role of silent mating type information regulation 2 homologue 1 (SIRT1) in renal ischemia-reperfusion (IR) injury and its effect on nuclear factor-κB (NF-κB)-peroxisome proliferator-activated receptor gamma coactivator 1 alpha (PGC-1α) signal pathway in mice.

Methods: Animal models of renal ischemia-reperfusion injury were established in a total of 90 healthy male C57BL/6 mice. Determination techniques included routine biochemical methods for the levels of serum creatinine and blood urea nitrogen (BUN), spectrophotometry for the level of superoxide dismutase (SOD), H-E staining for the histological changes as well as immunohistochemical and Western blotting analyses for the expressions of SIRT1, NF-κBp65 and PGC-1α, respectively.

Results: Compared with that in control and sham-operated groups, the levels of serum creatinine and BUN were higher and SOD level in renal tissues were lower at 12 h and 24 h after reperfusion in IR groups (P < 0.05). H-E staining revealed evident pathological lesions including necrosis of renal tubular epithelial cells in IR groups. Compared with the corresponding IR group, resveratrol attenuated the above-mentioned changes (P < 0.05) while EX527 aggravated those (P < 0.05). Both Western blotting and immunohistochemistry revealed the upregulated SIRT1 expression and the activated NF-κB signal pathway, the upregulated p65 expression and the downregulated PGC-1α expression subsequent to IR (P < 0.05). The expressions of SIRT1 and PGC-1α in resveratrol group were upregulated compared to that in IR group (P < 0.05) and the NF-κBp65 expression was downregulated (P < 0.05). While the SIRT1 and PGC-1α expressions in EX527 group were downregulated compared to that in IR group (P < 0.05) and the NF-κBp65 expression was upregulated (P < 0.05).

Conclusion: In mouse model of renal ischemia-reperfusion injury, the activation of SIRT1 could inhibit the NF-κBp65 expression and accordingly upregulated PGC-1α level, contributing to inhibited inflammatory reactions and attenuated oxidative stress-induced injury in the protection of the kidneys.

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0208
Vicious Circle of NLRP3 and Mitochondrial Damage Plays Central Role in Renal Ischemia-Reperfusion Injury
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Background: Tubular epithelial cells dysfunction and loss play a critical role in the evolution of ischemic AKI. Recent work suggested that mitochondrial damage and NLRP3 inflammasome activation are important drivers of AKI-associated pathology. And TXNIP, an endogenous inhibitor of the antioxidant thioredoxin and reactive oxygen species (ROS) sensor, may have a role in activating NLRP3 inflammasome.

Methods: C57BL/6J and NLRP3-/- male mice were subject to 30 minutes of ischemia and 1, 3, 7 days of reperfusion. We used mito-TEMPO, mitochondria-targeted antioxidant, to investigate whether NLRP3 inflammasome activation could be inhibited by reducing mitochondrial derived ROS (mROS). The mice were then sacrificed 1 day, 3 days or 7 days after renal ischemia reperfusion injury, and blood and tissues were harvested. In vitro study, we used a tubular epithelial cell line (HK-2). Cells were incubated for 1, 3, 6 or 9 hours of hypoxia-hyperglycemic plus 2 hours of normoxia/normal-glucose incubation. Oxygen-glucose deprivation injury occurred by placing cells in a hypoxic environment (1% O2/5% CO2/94% N2) in the presence of glucose-free DMEM medium for 1, 3, 6 or 9 hours. Mitochondrial damage and the activation of NLRP3 were measured.

Results: In this study, we established an ischemia reperfusion induced-AKI model characterized by tubular epithelial cells damage, mitochondria dysfunction which led to the excessive production of mROS. The renal expression levels of the NLRP3, IL-1β and IL-18 were significantly increased in this animal model. However, kidney dysfunction and mitochondrial damage were attenuated obviously in NLRP3-/- mice compared with WT mice with ischemia AKI. In vitro, oxygen-glucose deprivation injury timely dependent increased the expression levels of NLRP3 inflammasome axis. The mitochondrial injury in damaged HK2 cells was also suppressed by silencing NLRP3 and caspase1.

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