0085 Proteomics and Metabolite Analysis Reveals the Role of hnRNP K in HK2 Cells

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Background: Salt sensitive hypertension is a kind of metabolic syndrome. HnRNP K was up-regulated in renal medulla of salt resistant rats, but down-regulated in salt sensitive rats and the latter developed hypertension. The function of hnRNP K in renal cells of salt sensitive hypertension rats is not fully understood.

Methods: Proteomics and metabolomics profiling, Western blot, biochemistry analysis and ATP generation rate detection were used to figure out the global regulatory functions of hnRNP K in HK2 cells through siRNA knockdown technology.

Results: The proteomics analysis indicated that the expression of multiple enzymes in mitochondrial were increased while hnRNP K was knocked down, such as MDH, PDH, α-KGDH, NADH dehydrogenase, cytochrome b-c1 complex, cytochrome c and ATP synthase, of which, MDH, PDH, cytochrome c were further verified by western blot. The activities of MDH, FH, α-KGDH and mitochondria NADP-ICD were also increased. Bioinformatic analysis revealed that glycolysis/gluconeogenesis was decreased and TCA and oxidative phosphorylation pathway were significantly increased. The results suggested that the function of mitochondrial improved, which were confirmed by the increasing of membrane potential and ATP generation rate when hnRNP K was knocked down. Further detection of metabolic intermediates by GC/MS showed succinate, malate, lactate acid, 11 amino acids which could transform to substrates of TCA were decreased in hnRNP K knockdown cells except pyruvate. The change of metabolic compounds confirmed the results of bioinformatic analysis.

Conclusion: Consequently, current research work demonstrated that down-regulated hnRNP K contributes to enhanced protein expression of the TCA cycle and oxidative phosphorylation, but depresses glycolysis/gluconeogenesis in kidney cells. These data also suggested that the regulatory function of HnRNP K to metabolism of mitochondrial could be involved in the development of salt induced hypertension.

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0117 Hypertension in Non-dialysis CKD Patients in China

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Objective: The aim of the present study was to investigate the prevalence, awareness, treatment, and control of hypertension in the non-dialysis CKD patients through a nationwide, multicenter study in China.

Methods: The survey was performed in 61 tertiary hospitals in 31 provinces, municipalities, and autonomous regions in China (except Hong Kong, Macao, and Taiwan). Trained physicians collected demographic and clinical data and measured blood pressure (BP) using a standardized protocol. Antihypertensive drugs were classified into a single category and the percent of every category were counted. Resistant hypertension was defined as BP above the target BP (<140/90 mmHg) despite the use of 3 antihypertensive drugs or achieving the target BP by using ≥4 antihypertensive drugs.

Results: The analysis included 8927 non-dialysis CKD patients. The prevalence, awareness, and treatment of hypertension in non-dialysis CKD patients were 67.3%, 85.8%, and 81.0%, respectively. Of hypertensive CKD patients, 33.1% had controlled BP to <140/90 mmHg. In 4435 participants who had records of antihypertensive treatment, 36.9% achieved hypertension control, 11.1% met the criteria for resistant hypertension and 52.0% used <2 antihypertensive drugs and were uncontrolled.

Conclusion: The prevalence of hypertension Chinese non-dialysis CKD patients was high, and the hypertension control was suboptimal. Compared to resistant hypertension, the inadequate use of antihypertensive drugs appeared to contribute more to the lack of hypertension control in CKD patients.

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0205 Role of Mitochondrial Dysfunction and ROS Production in Ang II-induced NLRP3 Inflammasome Activation

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Objective: The type 1 angiotensin (AT1) receptor plays an important role in maintaining blood pressure. Previous studies suggested that the activation of immune responses by angiotensin (Ang) II during hypertension may aggravate renal damage. NLRP3 inflammasome activation promotes renal inflammation and contributes to chronic kidney damage. Further investigation should be performed to explore the correlation between the RAS and NLRP3 inflammasome activation, and possible mechanisms.

Methods: C57BL/6 AT1R-/- and NLRP3-/- mice underwent left nephrectomy followed 1 week for recovery. Blood pressure measurements were recorded at baseline and following 4 weeks of chronic Ang II or saline infusion. At the end of the experiment, the kidney were harvested and fixed. AT1R siRNA and mitoTEMPO treatment were performed before the Ang II stimulation in HK2 cells. The expression levels of NLRP3 inflammasome and mitochondrial dysfunction were measured.

Results: Ang II significantly induced kidney injury and NLRP3 inflammasome activation. Mitochondria swelling and fragmentation were observed by transmission electron microscope. AT1-/- blocked Ang II-induced hypertension, inhibiting the mitochondrial dysfunction and NLRP3 expression. Deficiency of NLRP3 attenuated kidney injury in hypertension with no significant influence to blood pressure. In vitro studies showed that Ang II stimulation increased the mitochondrial damage and NLRP3 activation in dose- and time-
dependent manner. AT1R silence effectively blocked Ang II-induced damage. MitoTEMPO attenuated the activation of NLRP3 inflammasome through clear- ance of reactive oxygen species (ROS). Moreover, Ang II-induced mitochondrial dysfunction was markedly inhibited by silence of NLRP3.

Conclusion: Ang II stimulation induces NLRP3 inflammasome activation through AT1a receptor. Ang II-induced NLRP3 activation is mediated by mito- chondrial dysfunction, with overproduction and accumulation of ROS. NLRP3 inflammasome activation plays an important role in kidney injury, and block- ing it can be a potential therapeutic target for hypertension-associated kid- ney damage.

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0220
International Congress of Chinese Nephrologists: Clinical and Pathological Characteristics of 75 Chinese Patients with Benign Hypertensive Nephrosclerosis
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Objective: To identify the clinical and pathological characteristics of 75 Chi- nese patients with benign hypertensive nephrosclerosis (BHN) and the rela- tionship between the clinical and pathological changes.

Methods: BHN patients proved by renal biopsy were retrospectively analyzed based on the clinical and pathological records. Glomerular lesions were divided into five types: hypertrophic, focal segmental sclerotic, solid- ified or ischemic (including wrinkled and obsolete changes). Patients were grouped for further analysis according to whether eGFR > 60 ml/min/1.73 m², > 30% ischemic glomeruli, > 20% obsolete glomeruli, respectively.

Results: 75 BHN patients with an average age of 44.4 ± 10.7 years, M/F 4:1. eGFR had significant negative correlation with systolic blood pressure (SBP) (r = -0.276, P = 0.016) but not diastolic blood pressure (DBP). DBP had sig- nificant negative correlation with age (r = -0.3, P = 0.007). The most common pathological type of glomerular lesion was ischemic (30.6%), including ischemic wrinkled (13%) and obsolete (17.6%). Arteriolar stenosis had sig- nificant positive correlation with ischemic glomerular lesion (r = 0.33, P = 0.004), but not obsolete glomeruli. Multivariate analysis showed: (1) SBP rather than DBP was independent risk factor of eGFR decline; (2) in- dependent associated factors of ischemic glomerular change were TG (OR = 1.78, 95% CI 1.02–3.1; P = 0.041), age (OR = 0.93, 95% CI 0.89–0.99; P = 0.018) and eGFR (OR = 0.97, 95% CI 0.95–0.99; P = 0.004); (3) independent associated factors of obsolete glomeruli were TG (OR = 1.96, 95% CI 1.13–3.4; P = 0.016) and eGFR (OR = 0.97, 95% CI 0.95–0.99; P = 0.012).

Conclusion: SBP is independent risk factor of eGFR decline in BHN. TG pro- moted the development of ischemic and obsolete glomerular lesion which may offer a new therapeutic target for the management of BHN.

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0235
Risk Factors and Their Interaction on CKD In Patients with Hypertension and DM: A Multicenter Case Control Study in Taiwan
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Objective: Chronic kidney disease (CKD) is highly prevalent in Taiwan. More than two-thirds of end-stage renal disease is associated with diabetes mellitus (DM) or hypertension (HTN). Therefore, the formulation of a special preventative policy of CKD in these patients is essential. This study surveyed 14 traditional risk factors and identified their effects on CKD in patients with HTN/DM and compared these with their effects in the general population.

Methods: This study included 5328 cases and 5135 controls in the CKD-HTN/ DM outpatient centers of 10 hospitals in Taiwan. Fourteen common effect factors were surveyed (four demographic, five disease and five lifestyle), and their effects on CKD were tested. Significance tests were adjusted by the Bonferroni method. Results of the stratified analyses in the variables were presented with significant heterogeneity between patients with different comorbidities.

Results: Male, ageing, low income, hyperuricemia and lack of exercise habits were risk factors for CKD, and their effects in people with different comorbidities were identical. Anemia was a risk factor, and there was an ad- ditive effect between anemia and HTN on CKD. Patients with anemia had a higher risk when associated with HTN [odds ratio (OR) = 6.75, 95% CI 4.76–9.68] but had a smaller effect in people without HTN (OR = 2.83, 95% CI 2.16–3.67). The association between hyperlipidaemia-related factors and CKD was also moderated by HTN. It was a significant risk factor in people without HTN (OR = 1.67, 95% CI 1.38–2.01) but not in patients with HTN (OR = 1.03, 95% CI 0.89–1.19). Hepatitis B, hepatitis C, betel nut chewing, smoking, alcohol intake and groundwater use were not associated with CKD in multivariate analysis.

Conclusion: We considered that patients with HTN and anemia were a high CKD risk population. Physicians with anemic patients in outpatient clinics need to recognize that patients who have HTN might be latent CKD cases.

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