論文發表注意事項

【口頭論文發表】

- 試片室：7 樓 701C 會議室及 701G 會議室外小房間
- 口頭報告者請務必於該場次開始前 30 分鐘將隨身碟自行攜帶送至試片室進行測試，以避免中途影響會議速度進行，請先行測試檔案與隨身碟讀取正常。
- 一般論文口頭發表，每題 12 分鐘(報告 10 分鐘，討論 2 分鐘)，請各演講者務必控制報告時間，演講時間結束後即開燈結束演講。
- 學會於90年新增『年會論文優秀論文獎』，口頭發表及壁報發表分別評分。優秀論文獎得獎名單於會員大會公佈並頒獎。
- 得獎公佈—會員大會
  時間：112 年 12 月 10 日(星期日)上午 11:30 至 12:00 (請得獎者務必在現場)
  地點：701B會議室

- Our Preview Room are located outside of conference rooms 701B and 701F
- ***Oral Presentation***

Presentation Time
12 Minutes: including 10 minutes of presentation and 2 minutes of Live Q&A
Presentation Specification
***All oral presentation must Present LIVE.** File Type: **PPT or PPTX** only File Name: Oral_AbstractID_Name (e.g: OralPresentation1_25_Lin)

Oral Presentation 2 (Chinese)

December 9 (Saturday), 2023 09:00 ~ 10:30 Room 5 (702)

【Basic-2】 *Chair(s)：許翔皓/ Hsiang-Hao Hsu、楊智宇/ Chih-Yu Yang*

09:00—09:12

1. Decreased NK cell-mediated cytotoxicity is associated with hypoalbuminemia in hemodialysis patients
Bing-Rong Chung[1], Kai-Hsiang Shu[1], I-Yu Chen[1], Yen-Ling Chiu[1,2,3]
[1]Division of Nephrology, Department of Medicine, Far Eastern Memorial Hospital
[2]Graduate Institute of Medicine, Yuan Ze University
[3]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine

09:12—09:24

2. Activation of hypoxia-inducible factors in erythroid progenitor cells results in defective erythropoiesis
Szu-Yu Pan[1], Pei-Zhen Tsai[2], Shuei-Liong Lin[1,2]
[1]National Taiwan University Hospital, [2]Graduate Institute of Physiology, National Taiwan University College of Medicine

09:36—09:48

4. Molecular mechanisms of thiazide diuretics-mediated inhibition of the sodium-chloride cotransporter
Chien-Ling Lee[1,2], Minrui Fan[1,2], Jianxiu Zhang[1,2], Jinru Zhang[1,2] & Liang Feng[1]
[1]Department of Molecular and Cellular Physiology, Stanford University School of Medicine, Stanford, CA, USA. [2]These authors contributed equally

09:48—10:00

5. The protective effect of Visnagin on LPS-induced acute kidney injury via NF-kB pathway and antioxidative pathway
Sheng-Wen Wu[1,2], Yu-Hsiang Kuan[3]
[1]School of Medicine, Chung Shan Medical University, Taichung, Taiwan
[2]Division of Nephrology, Chung Shan Medical University Hospital, Taichung, Taiwan
[3]Department of Pharmacology, School of Medicine, Chung Shan Medical University, Taichung, Taiwan

10:00—10:12

6. Protective Role of Taurine on Rat Offspring Hypertension in the Setting of Maternal Chronic Kidney Disease
You-Lin Tain[1], Wei-Ling Chen[1], Wei-Ting Liao[1], Chien-Ning Hsu[2]
[1]Division of Pediatric Nephrology and [2]Department of Pharmacy, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

Oral Presentation 2 (Chinese)

December 9 (Saturday), 2023 09:00 ~ 10:30 Room 5 (702)

10:12-10:24

7. Impact of Irisin Deficiency on Podocytopathy and Diabetic Kidney Disease in a Murine Model

Hsin-Hung Chen, Tzu-Ming Jao, Chia-Jung Li, and Jin-Shuen Chen
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【Oral Presentation 2】
【Basic-2】 Room 5 (702)

1

Decreased NK cell-mediated cytotoxicity is associated with hypoalbuminemia in hemodialysis patients

血液透析患者的低蛋白血症與自然殺手細胞功能異常相關

Bing-Rong Chung[1], Kai-Hsiang Shu[1], I-Yu Chen[1], Yen-Ling Chiu[1,2,3]

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Background：

The significance of Natural Killer (NK) cells in cancer immunity and immunotherapy has garnered substantial attention. Impaired NK cell function can severely compromise the host's immune system. End-stage kidney disease (ESKD) and hemodialysis (HD) are known among various factors contributing to NK dysfunction. Nonetheless, the precise mechanisms underpinning this phenomenon remain insufficiently elucidated.

Methods：

This study conducts a comprehensive multivariate and comparative analysis of NK cell subtypes and surface receptors across different age and gender categories in healthy populations. Furthermore, it compares these parameters in HD patients to healthy donors (HC). Additionally, NK cell cytotoxicity between HD patients and HC is assessed. The study also examines the biochemical data in HD patients with varying levels of NK cell cytotoxicity.

Results：

The analysis of NK cells in 44 HC reveals age-related increases in the proportions of total NK cells, CD56dim cells, and CD56dimCD16bright cells, accompanied by reductions in CD56bright cells and CD56dimCD16dim cells. Gender differences were not observed. Among 30 HD patients and 30 HC individuals, CD56bright cells increased, while CD56dim cells decreased in HD patients. HD patients exhibit reduced NK cell cytotoxicity across all four effectors: target ratios. Furthermore, a comparison within the HD patient group, distinguishing those with high and low cytotoxicity (7 in the former, 11 in the latter), reveals higher albumin levels in the high cytotoxicity group.

Conclusions：

This study uncovers significant functional disparities in NK cell cytotoxicity between HD patients and healthy individuals. Impaired cytotoxicity among HD patients is attributable to malnutrition, possibly mediated by hypoalbuminemia. This research is the first to elucidate the connection between serum albumin levels and NK cell dysfunction in ESKD.

Key words：

NK cells, hemodialysis, ESKD

2

Activation of hypoxia-inducible factors in erythroid progenitor cells results in defective erythropoiesis

在紅血球前驅細胞活化缺氧誘導因子造成紅血球生成異常現象

Szu-Yu Pan[1], Pei-Zhen Tsai[2], Shuei-Liong Lin[1,2]

潘思宇[1], 蔡佩蓁[2], 林水龍[1,2]

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[1]台大醫院, [2]台大醫學院生理學研究所

Background：

Hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI) activates HIF in renal pericytes and fibroblasts to promote erythropoietin production and erythropoiesis. However, the effects of HIF stabilization in the erythroid lineage are not clear. We aim to study the effects of erythroid lineage-specific stabilization of HIF on erythropoiesis by preclinical models.

Methods：

Epor$^{GFP\text{-}Cre/+}$*;Vhl*$^{F/F}$ mice were used to achieve erythroid lineage-specific stabilization of HIF. Surface expression of TER-119, CD44, and forward scatter (FSC) were used to define erythroblast, reticulocyte, and red blood cell in the bone marrow. Expression of propidium iodide and surface annexin V were used to define apoptosis. Stress erythropoiesis was induced by subcutaneous administration of phenylhydrazine.

Results：

Compared with littermate *Vhl*$^{F/F}$ mice, *Epor*$^{GFP\text{-}Cre/+}$*;Vhl*$^{F/F}$ mice had decreased hematocrit, decreased percentage of erythroblasts in the bone marrow, and increased apoptosis of erythroblasts in the bone marrow under steady state. These phenotypes of defective erythropoiesis were normalized in mice harboring concomitant *Vhl*, *Hif1a*, and *Hif2a* deletion (*Epor*$^{GFP\text{-}Cre/+}$*;Vhl*$^{F/F}$*;Hif1a*$^{F/F}$*;Hif2a*$^{F/F}$ mice). Although macrophages in the bone marrow also express *Epor,* macrophage-specific *Vhl* deletion in either *Tg(Csf1r-CreESR1);Vhl*$^{F/F}$ or *Lyz2*$^{Cre/+}$*;Vhl*$^{F/F}$ mice did not result in defective erythropoiesis. During stress erythropoiesis, compared with littermate *Vhl*$^{F/F}$ mice, *Epor*$^{GFP\text{-}Cre/+}$*;Vhl*$^{F/F}$ mice had similar hematocrit, lower percentage of erythroblast in the bone marrow, and increased percentage of erythroblast in the spleen.

Conclusions：

Vhl deletion in erythroid progenitor cells impairs erythropoiesis in murine bone marrow in the steady state. The phenotypes of defective erythropoiesis were partially reversed during stress erythropoiesis.

Key words：

Hypoxia-inducible factor, erythroid progenitor cell, erythropoiesis

4

Molecular mechanisms of thiazide diuretics-mediated inhibition of the sodium-chloride cotransporter

Chien-Ling Lee[1,2], Minrui Fan[1,2], Jianxiu Zhang[1,2], Jinru Zhang[1,2] & Liang Feng[1]

[1]Department of Molecular and Cellular Physiology, Stanford University School of Medicine, Stanford, CA, USA. [2]These authors contributed equally.

Background:

Thiazide diuretics are important first-line antihypertensive drugs and function by inhibiting the sodium-chloride cotransporter (NCC) in the distal convoluted tubule. However, off-target metabolic adverse effects, including impaired glucose tolerance and dyslipidemia, limit the clinical usage of thiazide diuretics. The knowledge of mechanisms of thiazide diuretics-mediated NCC inhibition will aid in the development of next-generation NCC inhibitors with fewer side effects.

Methods:

Detergent purified chimeric human NCC ($hNCC_{chimera}$), with the N-terminal domain of hNCC replaced with that of zebrafish NKCC1, and its extracellular gate mutation (E240A) variant copurified with polythiazide were subjected to cryogenic electron microscopy (cryo-EM) for structural determination of the apo and polythiazide-bound states, respectively. A human embryonic kidney 293 cell-based radioactive iodide uptake assay was used for functional characterization of hNCC variants.

Results:

We determined the cryo-EM structures of $hNCC_{chimera}$ and $hNCC_{chimera}$(E240A) in complex with polythiazide at 3.0 Å and 2.8 Å resolutions, respectively. The transmembrane domain (TMD) of $hNCC_{chimera}$ adopts an inward-facing conformation. In contrast, the TMD of $hNCC_{chimera}$(E240A) in complex with polythiazide adopts an outward-facing conformation with a vestibule extending from the extracellular space to the center of the TMD. Polythiazide binds to the bottom of the vestibule with its 7-position sulfamoyl group pointing downward. Polythiazide forms extensive interactions with NCC, and alanine substitutions of key interacting residues drastically reduced NCC affinity for polythiazide. Our structures reveal two mechanisms of polythiazide-mediated NCC inhibition. First, polythiazide competes with chloride (Cl^-) binding as its 6-position chlorine group occupies NCC Cl^--binding site. Second, polythiazide binding prevents NCC conformational transitions as the movement of transmembrane helix 10 would clash with polythiazide if NCC switched from an outward- to an inward-facing conformation.

Conclusions:

Cryo-EM structures of NCC alone and in complex with polythiazide disclose that polythiazide inhibits NCC through 1) competitive inhibition and 2) conformational transition stalling.

Key words:

Sodium-chloride cotransporter (NCC); thiazide diuretics; cryogenic electron microscopy (cryo-EM)

5

The protective effect of Visnagin on LPS-induced acute kidney injury via NF-kB pathway and antioxidative pathway

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Background : In consideration of high mortality rates of sepsis-induced acute kidney injury (S-AKI) even in modern era, to clarify the underlying pathogenic mechanisms and develop the effective therapeutic strategies of AKI are unmet needs. Visnagin, one of the active components of ginseng, has been proved to possess antimicrobial, anti-inflammatory, analgesic, and renal vasodilatory effects. However, its efficacy in improving S-AKI has not been confirmed to date.

Methods: BALB/c mice were intraperitoneally pretreated with Visnagin for 30 min, and then LPS injection was applied to induce AKI for 24 h. Blood samples were collected for biochemical assay. Kidney tissues were used for histopathology, enzyme-linked immunosorbent assay, and Western blot analyses.

Results: Visnagin not only dose-dependently attenuated histological damage and reduced renal myeloperoxidase expression but also decreased serum creatinine and blood urea nitrogen levels in LPS-treated mice significantly. Visnagin also markedly dose-dependently inhibited production of TNF-α, IL-1β, and IL-6 in renal tissue of LPS-treated mice via phosphorylation of nuclear factor-κB (NF-κB) p65. Moreover, Visnagin significantly dose-dependently reduced malondialdehyde (MDA) and increased activities of superoxide dismutase (SOD) and glutathione peroxidase (GPx) in renal tissue induced by LPS through upregulating expression of nuclear factor erythroid 2 related factor 2 (Nrf2).

Conclusion: These results suggest that Visnagin has protective effects against AKI in mice through regulating inflammation and oxidative stress.

6

Protective Role of Taurine on Rat Offspring Hypertension in the Setting of Maternal Chronic Kidney Disease

牛磺酸對慢性腎臟病母鼠後代高血壓的保護作用

You-Lin Tain,[1] Wei-Ling Chen,[1] Wei-Ting Liao,[1] Chien-Ning Hsu[2]
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Background: Taurine is a natural antioxidant with antihypertensive property. Maternal chronic kidney disease (CKD) has an impact on renal programming and increases risk for offspring hypertension in later life. The underlying mechanisms cover oxidative stress, dysregulated hydrogen sulfide (H2S) system, dysbiotic gut microbiota, and aberrant activation of the renin-angiotensin-aldosterone system (RAAS). We investigated whether perinatal taurine administration enables to prevent high blood pressure (BP) in offspring complicated by maternal CKD.
Methods: Before mating, CKD was induced through feeding chow containing 0.5% adenine for 3 weeks. Taurine was administered (3% in drinking water) during gestation and lactation. Four groups of male offspring were used (n=8/group): controls, CKD, taurine-treated control rats, and taurine-treated CKD rats. Male offspring were sacrificed at 12 weeks of age. Renal expression of H_2S-generating enzymes and RAAS components were analyzed by qPCR. Fecal samples were evaluated by full-length 16S rRNA gene-based metagenomics analysis.
Results: Perinatal taurine treatment targets renal programming to halt its adverse programming processes, helping to prevent adult offspring against hypertension and renal hypertrophy. Taurine supplementation increased gene expression of H_2S-producing enzymes and H_2S production in offspring's kidneys. Additionally, taurine protected against offspring hypertension was coincided with the restoration of CKD-induced aberrant RAAS activation, characterized by decreases in renin, AGT, ACE, and AT1R expression. Moreover, the beneficial effect of taurine is connected with an enhanced amount of the genera *Bifidobacterium*, *Asteroleplasma*, and *Dehalobacterium* and a decrease in *Erisipelactoclostridium*.
Conclusions: In conclusion, perinatal taurine administration has several protective effects on maternal CKD-induced offspring hypertension, covering the augmentation of H_2S system, rebalancing of the RAAS, and alterations in the gut microbiota. Our results not just deepen our knowledge of mechanisms underlying maternal CKD-induced offspring hypertension, but affords the impetus to consider taurine-based intervention as a promising preventive approach as well for future clinical translation.
Keywords: taurine; DOHaD; RAAS; CKD; gut microbiota; hypertension

7

Impact of Irisin Deficiency on Podocytopathy and Diabetic Kidney Disease in a Murine Model

鳶尾素缺乏對於足細胞病變和糖尿病腎病在小鼠模型中的影響

Hsin-Hung Chen, Tzu-Ming Jao, Chia-Jung Li, and Jin-Shuen Chen
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Background: Chronic kidney disease (CKD) is a significant global public health concern, with proteinuric kidney disease being a common manifestation. Podocytopathy, characterized by podocyte-related proteinuria, is a critical subtype of this disease, often categorized into diabetic and non-diabetic forms. Irisin, a myokine involved in various physiological processes, has been identified as a potential factor in CKD progression, particularly in diabetic contexts.
Objective: This study aims to elucidate the role of irisin in the pathogenesis of diabetic kidney disease and podocytopathy, focusing on its effects on renal function, proteinuria, and cellular apoptosis.
Methods: Utilizing CRISPR/Cas9 technology, we generated irisin-deficient mice within the C57BL/6 strain. These mice, alongside controls, were subjected to a high-fat diet and streptozotocin to induce diabetic kidney disease. We assessed the expressions of irisin and PGC1α, lipid peroxidation, and apoptosis in kidney, adipose, pancreas, and muscle tissues. Additionally, podocytopathy cell models were developed using glucotoxicity and albumin approaches to study the cellular impacts of high glucose and BSA treatment on mouse podocytes.
Results: Diabetic kidney disease in mice decreased irisin and PGC1α expressions and increased lipid peroxidation in multiple tissues. These effects were exacerbated in irisin knockout mice. The TUNEL assay indicated a significant increase in apoptosis in the kidneys of both diabetic and irisin-deficient mice, with a more severe effect observed in the combination group. In vitro, high glucose and BSA treatments reduced cell viability, apoptosis, cytoskeletal contraction, and mitochondrial fragmentation in mouse podocytes.
Conclusion: Our findings suggest that irisin deficiency exacerbates the pathological effects of diabetic kidney disease, implicating irisin as a potential therapeutic target. The observed alterations in irisin and PGC1α expressions, lipid peroxidation, and apoptosis highlight the complex interplay between metabolic factors and kidney pathology in diabetic contexts. Further research is warranted to explore the therapeutic potential of irisin modulation in diabetic kidney disease and podocytopathy.