Oral Presentation (Chinese)

December 14, 2024 (Saturday) 10:30 ~ 12:00 Venue：Room 5 (第四講堂)

【Oral-5】 Chair(s)：黎思源/ Szu-Yuan Li、鄭本忠/ Ben-Chung Cheng

10:30—10:42

1. LncRNA ATP6V0E2-AS1 Regulates Mitophagy through PINK1 in Renal Tubular Cells under Hypoxia Condition

I-Kuan Wang[1,2], Tung-Min Yu[2,3], Ya-Wen Chuang[2,3], Chi-Yuan Li[2,3]
[1] Divisions of Nephrology, China Medical University Hospital, Taichung, Taiwan, [2]Department of Medicine, College of Medicine, China Medical University, Taichung, Taiwan, [3] Department of Anesthesiology, China Medical University Hospital, Taichung, Taiwan

10:42—10:54

2. Mesothelial Cells on Aligned Nanofiber web Scaffolds for Mesothelial Tissue Engineering

Hao-Hsi Kao[1], Chang-Yi Kuo[2], Darshan Tagadur Govindaraju[3], Kuo-Su Chen[4], Jyh-Ping Chen[5]
[1] Division of Nephrology, Chang Gung Memorial Hospital at Keelung, Keelung, [2] School of Medicine, College of Medicine, Chang Gung University, [3] Department of Chemical and Materials Engineering, Chang Gung University

10:54—11:06

3. TREM-1 Mediates Inflammation and Vascular Calcification Following Chronic Kidney Disease

Chien-Liang Chen[1,2,3], En-Shao Liu[1], Chih-Yang Hsu[1,2,3], Hsin-Yu Chen[1,2], Po-Tsang Lee[1,2], Tsu-Yuan Chang[1,2], Chien-Wei Huang[1,2], Hua-Chang Fang[1,2], Jin-Shuen Chen[1]
[1]Kaohsiung Veterans General Hospital, Division of Nephrology, [2] National Yang Ming Chiao Tung University, [3] National Sun Yat-sen University

11:06—11:18

4. The Role of *FNDC5*/Irisin Deficiency in Exacerbating Mitochondrial Dysfunction and Diabetic Nephropathy

Chien-Wei Haung[1,2], Hsin-Hung Chen[3], Tzu-Ming Jao[4], Chia-Jung Li[3], Chian-Huei Guo[3], Junne-Ming Sung[2] Yau-Sheng Tsai[2,*], Jin-Shuen Chen[5,*]
[1]Division of Nephrology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; [2]Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [3]Dpartment of Medical Education and Research, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; [4]Global Innovation Joint Degree Program, International Joint Degree Master's Program in Agro-Biomedical Science in Food and Health, College of Medicine, National Taiwan University, Taipei, Taiwan; [5]Department of Administration, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan

11:18—11:30

5. The Impact of Balance Solution on The Outcomes of Incident Peritoneal Dialysis Patients

Ming-Hsien Lin[1], Cheng-Li Lin[2], Ping-Chin Lai[1,3], I-Kuan Wang[1,3]
[1]Division of Nephrology, China Medical University Hospital, Taichung, Taiwan, [2]Magement Office for Health Data, China Medical University Hospital, Taichung, Taiwan, [3]School of Medicine, China Medical University, Taichung, Taiwan

11:30—11:42

6. Kidney Outcome with SGLT2 Inhibitor Versus DPP4-Inhibitors Use in Type 2 Diabetes Adults with Obesity

Ho-Hsiang Chang[1], Tzu-Shan Huang[2], Jo-Yen Chao[2], Wei-Ren Lin[2], Chen-Yi Yang[3], Huang-Tz Ou[34], Wei-Hung Lin[2]
[1.] Division of Nephrology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan. [2.] Department of Internal Medicine, College of Medicine, National Cheng Kung University Hospital, National Cheng Kung University, Tainan, Taiwan. [3.] Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan

1

LncRNA ATP6V0E2-AS1 regulates mitophagy through PINK1 in renal tubular cells under hypoxia condition

長鏈非編碼核糖核酸 ATP6V0E2-AS1 在缺氧腎小管細胞藉由調控 PINK1 來影響粒線體自噬

I-Kuan Wang[1,2], Tung-Min Yu[2,3], Ya-Wen Chuang[2,3], Chi-Yuan Li[2,3]
王怡寬[1,2], 游棟閔[2,3], 莊雅雯[2,3], 李繼源[2.,4]
[1] Divisions of Nephrology, China Medical University Hospital, Taichung, Taiwan, [2]Department of Medicine, College of Medicine, China Medical University, Taichung, Taiwan, [3] Department of Anesthesiology, China Medical University Hospital, Taichung, Taiwan
[1] 中國附醫腎臟科, [2] 中國醫藥大學醫學院, [3] 台中榮總腎臟科,[4] 中國附醫麻醉科

Background: Mitophagy activation is crucial for hypoxia signaling in acute kidney injury (AKI). Selective removal of damaged mitochondria is mediated through a concerted function of coding and non-coding RNA expressions. Insights on HIF-1α signaling in lncRNA-regulated mitophagy mechanism are not known. The study aims to investigate the role of hypoxia-inducible factor 1α (HIF-1α) regulated long non-coding RNA (lncRNA) ATP6V0E2-AS1 in acute kidney injury (AKI) by examining its effect on mitophagy.

Methods: Mitophagy proteins (PINK1, p-PARKIN, LC3) were determined through western blot analysis. Immunofluorescence studies of PINK1 mitochondrial translocation and LC3/TOMM20 localization were determined using confocal analysis. HIF-1α interaction with lncRNA-ATP6V0E2-AS1 through promoter binding activity was evaluated through chromatin immunoprecipitation analysis. RNA interaction between lncRNA-ATP6V0E2-AS1 and PINK1 was analyzed by dual-luciferase reporter assay.

Results: Hypoxia upregulated PINK1, p-PARKIN, LC3 expressions, and mitophagosome in HK-2 cells. Bioinformatics, and real-time PCR are used to identify the candidate lncRNA ATP6V0E2-AS1. Overexpression and knockdown studies of hypoxia-regulated lncRNA-ATP6V0E2-AS1 significantly regulated PINK1/p-PARKIN expressions, subsequent PINK1 mitochondrial co-localization, and mitophagosome formation. shHIF-1α knockdown in HK-2 cells reveals that HIF-1α mediates PINK1/p-PARKIN mitophagy regulation under hypoxic conditions. In detail, HIF-1α binds to the promoter of lncRNA-ATP6V0E2-AS1 and down-regulates its expression under hypoxia. Deficiency of both HIF-1α and lncRNA-ATP6V0E2-AS1 reverted shHIF-1α mediated suppression of PINK1 expression and mitophagosome formation. Further, ATP6V0E2-AS1 post-transcriptionally regulates PINK1 expression by RNA-RNA interaction.

Conclusion: Altogether, our study shows novel findings on the HIF-1α mediated lncRNA-ATP6V0E2-AS1 in hypoxia-induced mitophagy regulation in the renal tubular cells. Thus, downregulated ATP6V0E2-AS1 expression with subsequent mitophagy activation is critical for hypoxia-induced mitophagy regulation through HIF-1α/ATP6V0E2-AS1/PINK1 axis.

Key words: Mitophagy; lncRNA; ATP6V0E2-AS1; PINK1; Acute kidney injury; HIF-1α

2

Mesothelial Cells on Aligned Nanofiber web Scaffolds for Mesothelial Tissue Engineering

探討間皮組織工程的對齊奈米纖維網支架上間皮細胞的培養

Hao-Hsi Kao[1], Chang-Yi Kuo[2], Darshan Tagadur Govindaraju[3], Kuo-Su Chen[4], Jyh-Ping Chen[5]
高皓璽[12], Darshan Tagadur Govindaraju[3], 陳志平[3]
[1] Division of Nephrology, Chang Gung Memorial Hospital at Keelung, Keelung [2] School of Medicine, College of Medicine, Chang Gung University [3] Department of Chemical and Materials Engineering, Chang Gung University
[1] 基隆長庚腎臟科 [2] 長庚大學醫學系 [3] 長庚大學化工暨材料研究所

Background：
A previous study indicated that mechanical loading could maintain the phenotype and innate elongated cell morphology of tenocytes to increase expression of tendon-specific genes as well as synthesis of marker proteins. The normal abdominal wall is in an intermittent stretched state, so we use the tensile status to cultivate cells. In vitro, via this biophysical beacon from mechanical loading, dynamic cell culture may increase cell proliferation rate and cell phenotype maintenance compared to static culture. Specifically, due to the unique anisotropic structure and biomechanical properties of peritoneum, the ideal scaffold for mesothelial tissue engineering should have a similar form and possess comparable physical properties that can improve the quality of engineered mesothelial tissue.
Methods：
For random nanofibers, the nanofibers were collected with a grounded static collector covered with aluminum foil. For aligned nanofibers, a grounded rotational drum covered with aluminum foil was used at 2500 rpm rotation rate. An aliquot of 10 μl of a cell suspension (10^7 cells/ ml) is seeded onto the surface of the electrospun web. In vitro SEM analysis, DNA quantification, and quantitative real-time polymerase chain reaction (qPCR) were used to examine and further discuss cell viability, morphology, and gene performance on the network.
Results：
The aligned configuration demonstrated a significantly higher count of mesothelial cells compared to the random configuration at both time points. From the SEM observations of the cell-seeded scaffolds, the mesothelial cells were mostly polygonal in shape, resembling a typical cobblestone pattern of mesothelial cells, on day seven. Comparing day three and seven, the cells became more elongated, but the general phenotype remained. More cells, together with their secreted ECM, were also found to attach to the surface on day seven. The quantitative real-time polymerase chain reaction (qRT-PCR) to quantify the relative (normalized to day 1) gene expression levels of calretinin, E-cadherin, vascular endothelial factor (VEGF), and intercellular adhesion molecule (ICAM-1) by mesothelial cells in GHCS random and aligned nanofiber membrane scaffold. The glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as a control
Conclusions：
The structure of the aligned webs produced more mimic the topology and porosity of basal lamina. The porosity of electrospun webs seems too small to provide enough space for cell ingrowth. In addition to its low toxicity, biodegradability, and biocompatibility, chitosan is also known for its similarity to ECM, which results in positive effect on cell growth, so the PCL/chitosan composite web was fabricated. The culture of mesothelial cells in the aligned webs makes the performance of mesothelial marker genes significantly better than random webs.
Choosing the aligned webs for in vivo studies, the cell/web construct was used for the transplantation of allograft mesothelial cells for mesothelium reconstruction in rats. A mesothelium layer similar to the native mesothelium tissue could be obtained 7 days post-implantation, based on H&E and IHC staining.
Key words：
Mesothelial cell, Aligned nanofibers , Polycaprolactone, Chitosan, Electrospinning

3

TREM-1 Mediates Inflammation and Vascular Calcification Following Chronic Kidney Disease

骨髓細胞上表現的觸發受體-1 調控慢性腎臟病後的血管發炎和鈣化

Chien-Liang Chen[1,2,3], En-Shao Liu[1], Chih-Yang Hsu[1,2,3], Hsin-Yu Chen[1,2], Po-Tsang Lee[1,2], Tsu-Yuan Chang[1,2], Chien-Wei Huang[1,2], Hua-Chang Fang[1,2], Jin-Shuen Chen[1]
陳建良[1,2,3], 劉恩紹[1], 許智揚[1,2,3], 陳信佑[1,2], 鍾東玲[1,2], 李柏蒼[1,2], 張子爰[1,2], 黃建維[1,2], 方華章[1,2], 陳金順[1]
[1]Kaohsiung Veterans General Hospital, Division of Nephrology, [2] National Yang Ming Chiao Tung University, [3] National Sun Yat-sen University
[1] 高雄榮民總醫院 [2] 國立陽明交通大學 [3] 國立中山大學

Background：

Vascular calcification, is an important risk factor for cardiovascular events in chronic kidney disease (CKD) patients. A growing body of research indicated that innate immunity and sterile inflammation plays a pivotal role in the pathogenesis of cardiovascular disease. A receptor of the immunoglobulin superfamily, triggering receptors expressed on myeloid cells-1 (TREM-1) was shown to amplify the sterile inflammation of cardiovascular disease, which hence makes it is possible as an important factors of vascular calcification in patients with CKD.

Methods：

In this study, we examined the role of triggering receptor expressed on myeloid cells-1(TREM-1) in orchestrating the inflammatory response that follows CKD process by invitro and invivo studies (animal and clinical studies).

Results：

High phosphate medium could increase the TREM-1 mRNA expression of rat vascular smooth muscle cells. After CKD, TREM-1 expression is upregulated in the vascular wall of Rat and Humans. There are also increased numbers of CD 68 cells with TREM-1 colocalization in the vascular walls in the CKD models. The soluble form of TREM-1 (sTREM-1), a marker of TREM-1 activation, is detectable in the serum of patients having end stage renal disease under hemodialysis, and its concentration are correlated with the severity of vascular calcification. TREM-1 pharmacological inhibition using a synthetic peptide (LP17) dampens invitro rat vascular cells osteogenic trans differentiation and vascular calcification of CKD rat models, limits inflammatory cells recruitment to the vascular walls.

Conclusions：

These data suggest that TREM-1 could constitute a new therapeutic target of vascular inflammation and cardiovascular disease during CKD process.

Key words：

TREM-1; innate immunity; Inflammation; vascular calcification; chronic kidney disease.

4

The Role of *FNDC5*/Irisin Deficiency in Exacerbating Mitochondrial Dysfunction and Diabetic Nephropathy

鳶尾素缺乏在加重粒線體功能障礙與糖尿病腎病變中的作用機制

Chien-Wei Haung[1,2], Hsin-Hung Chen[3], Tzu-Ming Jao[4], Chia-Jung Li[3], Chian-Huei Guo[3], Junne-Ming Sung[2] Yau-Sheng Tsai[2,*], Jin-Shuen Chen[5,*]
黃建維[1,2], 陳信宏[3], 饒梓明[4], 李佳榮[3], 郭千慧[3], 宋俊明[2], 蔡曜聲[2*], 陳金順[5*]
[1]Division of Nephrology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; [2]Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [3]Dpartment of Medical Education and Research, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; [4]Global Innovation Joint Degree Program, International Joint Degree Master's Program in Agro-Biomedical Science in Food and Health, College of Medicine, National Taiwan University, Taipei, Taiwan; [5]Department of Administration, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan

Background：This study investigates the role of FNDC5/irisin in diabetic nephropathy (DN), focusing on mitochondrial function and oxidative stress responses in a murine T2DM model and examining the effects in mesangial cells and podocytes under high glucose conditions.

Methods：*FNDC5* knockout (KO) mice were generated using CRISPR/Cas9 and induced with T2DM through a high-fat diet and streptozotocin injection. Mitochondrial function, lipid peroxidation, and apoptosis markers were assessed in renal tissues. Additionally, cultured mesangial cells and podocytes were exposed to high glucose to evaluate irisin's protective effects on cellular structure, mitochondrial integrity, and function.

Results：*FNDC5* KO T2DM mice showed significant mitochondrial dysfunction in renal tissues, including elevated lipid peroxidation, reduced PGC-1α expression, and increased apoptosis. In mesangial cells, high glucose led to decreased *FNDC5* expression and impaired mitochondrial dynamics, with increased fission and reduced fusion gene expression, which were further exacerbated in *FNDC5*-deficient cells. Podocytes exposed to high glucose displayed disrupted mitochondrial morphology, increased oxidative stress, and fragmentation, which *FNDC5*/irisin appeared to mitigate by preserving mitochondrial structure and function.

Conclusions：*FNDC5*/irisin deficiency aggravates DN by intensifying mitochondrial dysfunction and oxidative stress in diabetic conditions, with specific impacts on mesangial cells and podocytes. These findings suggest that targeting *FNDC5*/irisin pathways may offer a therapeutic approach to mitigate DN progression by preserving mitochondrial integrity and cellular health.

Key words：
FNDC5, Irisin, Mitochondrial dysfunction, Lipid peroxidation, Apoptosis, Type 2 diabetes mellitus, Diabetic nephropathy.

5

The impact of balance solution on the outcomes of incident peritoneal dialysis patients

在腹膜透析病人使用 Balance 透析液的預後影響

Ming-Hsien Lin, MD[1], Cheng-Li Lin, MS[2], Ping-Chin Lai, PhD[1,3], I-Kuan Wang, PhD[1,3]
林明憲 [1], 林橙莉 [2], 賴彬卿 [1,3], 王怡寬 [1,3]
[1]Division of Nephrology, China Medical University Hospital, Taichung, Taiwan [2]Magement Office for Health Data, China Medical University Hospital, Taichung, Taiwan [3]School of Medicine, China Medical University, Taichung, Taiwan
[1] 中國醫藥大學附設醫院腎臟科, [2] 中國醫藥大學附設醫院健康資料管理辦公室, [3] 中國醫藥大學醫學系

Background：

The aim of the study is to investigate the effects of balance solution on the risks of technique failure, death, and the first episode of peritonitis in incident peritoneal dialysis (PD) patients.

Methods：

From the database of National Taiwan Health Insurance, newly diagnosed end-stage kidney disease patients receiving PD for at least 90 days from 2009 to 2020 were identified. These patients were grouped as balance solution users and balance solution non-users. The risks of death, technique failure and the first episode of peritonitis were compared between two cohorts by the end of 2020.

Results：

Compared to the non-users, the balance users had significant lower risks of technique failure (130.4 vs.173.3 per 1000 person-years; adjusted hazard ratio (HR) = 0.76, 95% confidence interval (CI) = 0.67-0.86) and mortality (159.6 vs. 193.6 per 1000 person-years; adjusted HR = 0.81, 95% CI = 0.73-0.91). However, the balance users had a significant higher risk of the first peritonitis episode (adjusted subhazard HR = 1.22, 95% CI = 1.05-1.41) with considering death as a competing risk, compared to non-users. The risk increased further in diabetic PD patients (adjusted subhazard HR = 1.46, 95% CI = 1.20-1.78).

Conclusions：

Balance solution was associated with lower risks of technique failure, and mortality, but an increased risk of the first episode of peritonitis.

Key words：

Balance solution; mortality; peritoneal dialysis; peritonitis; technique failure.

6

Kidney outcome with SGLT2 inhibitor versus DPP4-inhibitors use in type 2 diabetes adults with obesity

SGLT2 抑制劑與 DPP4 抑制劑對於肥胖第 2 型糖尿病成人患者的腎臟預後影響

Ho-Hsiang Chang[1], Tzu-Shan Huang[2], Jo-Yen Chao[2], Wei-Ren Lin[2], Chen-Yi Yang[3], Huang-Tz Ou[34], Wei-Hung Lin[2]

張賀翔[1], 黃子珊[2], 趙若雁[2], 林威任[2], 楊真怡[3], 歐凰姿[3], 林威宏[2]

[1.] Division of Nephrology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan. [2.] Department of Internal Medicine, College of Medicine, National Cheng Kung University Hospital, National Cheng Kung University, Tainan, Taiwan. [3.] Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

[1.] 佛教慈濟醫療財團法人花蓮慈濟醫院腎臟內科 [2.] 國立成功大學醫學院附設醫院內科部 [3.] 國立成功大學臨床藥學與藥物科技研究所

Background：

This study investigated whether SGLT2i (sodium-glucose cotransporter 2 inhibitor) is superior to DPP4i (dipeptidyl peptidase-4 inhibitors) among type 2 diabetes (T2D) patients with obesity.

Methods：

This retrospective cohort used electronic medical records from National Cheng Kung University Hospital, during 2015/1/1-2023/11/30. Adult T2D patients with obesity (BMI>=25) who stably prescribed SGLT2i or DPP4i from 2016/1/1 to 2023/5/31 were identified. The index date was defined as the first date of having SGLT2i or DPP4i. The composite renal outcomes and individual subtypes including progression to eGFR< 10 mL/min/1.73m^2, end-stage renal disease, renal transplant, and 40% declined of eGFR from baseline were considered as outcome of interests. After propensity score matching, the Cox propositional hazard model was performed to illustrate the relative prevention of renal events occurred between SGLT2i and DPP4i use presenting by hazard ratios with 95% confidence interval.

Results：

A total of 3,000 and 3,447 obese T2D patients were identified in the SGLT2i and DPP4i groups, respectively. SGLT2i group and DPP4i group were 1:1 matched by propensity score. Compared with 2192 patients in DPP4i group, 2192 patients in SGLT2i group had lower composite renal outcome (hazard ratio [HR], 0.66 [95% CI, 0.57-0.75]).

Conclusions：

SGLT2i-based regimens have the lower risk for composite renal outcomes, compared with DPP4i-based regimens in Taiwanese T2D patients with obesity.

Key words：

Obesity, Diabetes, Sodium-glucose cotransporter 2 inhibitor, Dipeptidyl peptidase-4 inhibitors.