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 1 (English)

December 9 (Saturday), 2023 09:00 ~ 10:30 Room 1 (701-A)

【Basic-1】 *Chair(s)：Sung Gyun Kim、Jung Tak Park、林水龍/ Shuei-Liong Lin*

09:00—09:12

1. Hypoxic Mesenchymal Stem Cells-Derived Exosomes Inhibit Renal Fibrosis through Modulating Heparin-Binding EGF-Like Growth Factor Signaling
Wei-Cheng Tseng[1,2,4], Shih-Chieh Hung[5], Der-Cherng Tarng[1,2,3,4,*]
[1]Division of Nephrology, Taipei Veterans General Hospital; [2]School of Medicine, [3]Department and Institute of Physiology, and [4]Center for Intelligent Drug Systems and Smart Bio-devices (IDS2B), National Yang Ming Chiao Tung University; [5]Institute of Biomedical Sciences, Academia Sinica

09:12—09:24

2. Integration of Molecular Docking and Solubility Analysis: Thymoquinone Derivatives as Dual-Action Agents for Chronic Kidney Diseases Targeting COX-1/2 Protein Receptors
RR Saputra[1], SM Ulfa[2]
[1]Department of Chemistry, Universitas Palangka Raya, Indonesia
[2]Department of Chemistry, University of Brawijaya, Indonesia

09:24—09:36

3. Mitochondrial dysfunction and autophagy blockade contribute to renal osteodystrophy in experimental chronic kidney disease-mineral bone disorder
Shun-Neng Hsu [1, 2], Louise A Stephen[1], Kanchan Phadwal[2], Roderick Carter[3], Ineke Luijten[3], Vicky E MacRae[2], Tom Freeman[4] and Colin Farquharson[2]
[1] Division of Nephrology, Department of Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan
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[4] The Janssen Pharmaceutical Companies of Johnson and Johnson, Pennsylvania, USA.

09:36—09:48

4. Modulatory Effects of Rubia cordifolia against some Blood Oxidative Stress Markers in diabetic Rats with chronic kidney disease
Shweta Katiyar
SBN Government PG College, Barwani (M.P), India

09:48—10:00

5. The therapeutic potential of Disintegrin ARGDRR in AKI to CKD continuum
Tsai-Chen Chiang[1], Jia-Huang Chen[1], Shao-Yu Yang[2], Jenq-Wen Huang[2], Kuan-Yu Hung[2], Tur-Fu Huang[4], Woei-Jer Chuang[5], Chih-Kang Chiang[1,2,3]
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[2]Division of Nephrology, Department of Internal Medicine, NTU Hospital
[3]Division of Blood purification, Department of Integrated Diagnostics & Therapeutics, NTU Hospital
[4]Graduate Institute of Pharmacology, College of Medicine, NTU
[5]Department of Biochemistry, National Cheng Kung University Medical College

Oral Presentation 1 (English)

December 9 (Saturday), 2023 09:00 ~ 10:30 Room 1 (701-A)

10:00—10:12

6. The Correlation of Hypercholesterolemia and Kidney Damage Status on High-Fat Induced Rats (Rattus Norvegicus) after Intervention of Synbiotic Drink Containing Lactobacillus sp. Isolates

B Melvern[1], AN Yosanto [2], HA Sudiarto[1]
[1] Bendan General Hospital, Pekalongan City, Central Java, Indonesia, [2]Aura Syifa Hospital, Kediri, East Java, Indonesia

10:12—10:24

7. Inhibition of angiopoietin-2 mitigates kidney injury by attenuating inflammation

An-Jie Luo[1], Fan-Chi Chang[2], Shuei-Liong Lin[1,2]
[1]Graduate Institute of Physiology, College of Medicine, National Taiwan University
[2]Renal Division, Department of Internal Medicine, National Taiwan University Hospital

【Oral Presentation 1】

Basic-1 **Room 1 (701-A)**

1

Hypoxic mesenchymal stem cells-derived exosomes inhibit renal fibrosis through modulating heparin-binding EGF-like growth factor signaling

缺氧間葉幹細胞外泌體藉調控肝素結合性上皮生長因子訊息以抑制腎纖維化

Wei-Cheng Tseng[1,2,4], Shih-Chieh Hung[5], Der-Cherng Tarng[1,2,3,4,*]

曾偉誠[1,2,4], 洪士杰[5], 唐德成[1,2,3,4*]

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Background：

Fibrogenesis is a critical determinant for progression of chronic kidney disease (CKD). Epidermal growth factor (EGF) signaling is implicated in the development of renal fibrosis. Hypoxic mesenchymal stem cells-derived exosomes (HMSC-exosomes) have been shown to protect against fibrotic diseases. Nonetheless, whether and how HMSC-exosomes inhibit renal fibrosis is unclear.

Methods：

Candidate profibrotic genes were identified by unbiased RNA sequencing from human renal biopsied tissue. The extent of renal fibrosis and profibrotic gene expression were investigated in the unilateral ureteral obstructed (UUO) mice kidneys and transforming growth factor-beta 1 (TGF-beta 1)-activated renal myofibroblasts with and without HMSC-exosomes treatment.

Results：

RNA sequencing unveiled that heparin-binding EGF-like growth factor (HBEGF) potentially promoted human renal fibrosis, and urine HBEGF levels were elevated in fibrotic CKD patients. HBEGF expression was also increased in murine UUO kidneys and renal myofibroblasts. Notably, HMSC-exosomes preferentially homed to injured kidneys, downregulated HBEGF, and suppressed renal fibrosis both in vivo and in vitro. Mechanistically, knockout of HBEGF by CRISPR-Cas9 in renal tubular cells further deciphered the pathogenic roles of HBEGF-Smad/mTOR signaling in renal fibrosis. A higher urine HBEGF level also predicted progressive renal function decline in CKD patients.

Conclusions：

HBEGF played a key profibrotic role in renal fibrogenesis and served as a novel biomarker for renal deterioration. HMSC-exosomes attenutated renal fibrosis through downregulating HBEGF signaling and could be applied to treat clinical fibrotic patients in the future.

Key words：

Exosome; heparin-binding EGF-like growth factor; hypoxic mesenchymal stem cells; renal fibrosis

2

Integration of Molecular Docking and Solubility Analysis: Thymoquinone Derivatives as Dual-Action Agents for Chronic Kidney Diseases Targeting COX-1/2 Protein Receptors

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[2]Department of Chemistry, University of Brawijaya, Indonesia

Background：

Chronic Kidney Diseases (CKD) pose a significant global health challenge, necessitating innovative therapeutic strategies. This study explores the potential of thymoquinone derivatives as dual-action agents for CKD treatment by employing a combination of molecular docking towards COX-1/2 protein receptors and an octanol-water solubility test.

Methods：

Thymoquinone derivatives were obtained by synthesizing from 2,6-dimethyl-1,4-benzoquinone via bromoalkyl (4,7,10 R-Br) reaction. Molecular docking simulations were performed toward COX-1 (ID 1EQG) and COX-2 (ID 1CX2). Additionally, the octanol-water solubility test was employed to evaluate the derivatives' physicochemical properties. Additionally, absorption, distribution, metabolism, excretion, and toxicity (ADMET) were predicted using SwissADME servers.

Results：

Target compounds were successfully synthesized. C7 activity has great binding affinity toward COX-1 and COX-2, respectively. Especially for the activity toward COX-1, the binding affinity of C7 was equal to Ibuprofen/native ligand (-7.7 kcal/mol). Otherwise, signaling activity of C7 toward COX-2 receptor in binding affinity showed -7.7 kcal/mol that slightly lower than SC-558/native ligand -11.3 kcal/mol. Additionally, according to solubility assay, C4, C7, and C10 showed good solubility and superior ADMET properties.

Conclusions：

In conclusion, novel benzoquinone (**C4, C7, C10**) could be considered as effective base materials as promising candidates for CKD treatment. Future studies encompassing in vitro and in vivo validations are warranted to corroborate these computational findings and propel these derivatives towards translational applications in CKD therapeutics.

Key words：

Chronic Kidney Diseases (CKD), Thymoquinone Derivatives, COX-1/2, Docking, Solubility, ADMET

3

Mitochondrial dysfunction and autophagy blockade contribute to renal osteodystrophy in experimental chronic kidney disease-mineral bone disorder

粒腺體及自噬體功能障礙致慢性腎臟病礦物質骨病變

Shun-Neng Hsu（許舜能）[1, 2], Louise A Stephen[1], Kanchan Phadwal[2], Roderick Carter[3], Ineke Luijten[3], Vicky E MacRae[2], Tom Freeman[4] and Colin Farquharson[2]

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[4] The Janssen Pharmaceutical Companies of Johnson and Johnson, Pennsylvania, USA.

Objectives: Chronic kidney disease–mineral and bone disorder (CKD-MBD) is a systemic disorder that presents with extra-skeletal calcification and renal osteodystrophy (ROD). The origins of ROD likely lie with the elevated levels of parathyroid hormone, fibroblast growth factor 23 (FGF23), and uremic toxins, but the complex bone-renal signaling pathways and cellular events they control during the development of ROD are unclear. To obtain an improved understanding of how this altered systemic milieu results in ROD, we used whole transcriptome sequencing (RNA-seq) to identify the molecular mechanisms responsible for the initiation and development of ROD.

Methods: To induce CKD-MBD, male C57BL/6 mice were fed a diet containing 0.6% calcium, 0.9% phosphate, and 0.2% adenine. RNA-seq analysis was completed on femurs at 5-day intervals over a 35-day course to identify temporal changes in gene expression with disease progression. The RNA-seq data was extended by examining mitophagy in bone from mito-QC reporter mice, human CKD patients, and murine primary osteoblasts challenged with the uremic toxin indoxyl sulfate (IS).

Results: CKD mice had the expected osteopenia, hyperphosphatemia, hyperparathyroidism, and elevated FGF23 circulating levels. RNA-seq analysis indicated a down-regulation of genes involved in mitophagy, mitochondrial function, and oxidative phosphorylation in the CKD-MBD mice and mito-QC mice provided direct evidence of mitophagy abnormalities. Immunoblotting of regulators of mitophagy (p62/SQSTM1, ATG7) in murine and human CKD bone provided evidence of delayed autophagic flux, which was also observed in IS-treated osteoblasts but reversible upon rapamycin treatment.

Conclusion: This is the first transcriptomic study of bone in an experimental model of CKD-MBD. Our findings are consistent with the hypothesis that mitochondrial dysfunction contributes to the altered bone remodeling characteristic of ROD. The full clinical implications of this conclusion are still to be determined.

Keywords: autophagy, mitophagy, bone, CKD-MBD, uremic toxins, renal osteodystrophy

4

Modulatory Effects of *Rubia cordifolia* against some Blood Oxidative Stress Markers in diabetic Rats with chronic kidney disease

Shweta Katiyar[1]

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Abstracts

Background：

Chronic kidney disease is the persistent and irreversible state of reduced renal capacity, which eventually leads to death when enough nephrons have been damaged. The most common cause of disease is diabetes, and the link between oxidative stress and diabetic induced renal failure has been addressed.

Recently for treating diabetes induced chronic kidney disease, natural products have attracted scientific researchers' attention such as manjishtha (*Rubia cordifolia*). In view of the antioxidant and anti-hyperglycemic properties of the manjishtha, the present study was carried out to evaluate its efficacy in affording protection against alloxan induced changes in rat kidney.

Methods：

The oxidative stress parameters as copper-zinc superoxide disumutase (CuZn SOD), glutathione peroxidase (GSH-Px), glutathione reducatase (GSSG-Rd), total GSH and GSSG were measured spectrophotometrically in kidney tissues. Additionally, ethanolic extract of plants was used to see the impact in diabetic rats and the effect was compared to that of glibenclamide.

Results：

A single intraperitoneal injection of alloxan (150 mg/kg) in rats produced hyperglycemia within 3 days and altered kidney functions over a period of 90 days. Daily oral administration of the plant extract (100 and 200 mg/kg) in diabetic rats produced anti-hyperglycemic effect that was comparable to that of glibenclamide (10 mg/kg). Unlike glibenclamide, the plant extract did not increase the serum insulin levels in diabetic rats. However, it produced a marked reduction in the levels of urinary glucose and protein and normalized the renal tissue levels of CuZn SOD, GSH-Px, GSSG-Rd, total GSH and GSSG in diabetic rats and the effect was comparable to that of glibenclamide.

Conclusions：

The findings suggested that an imbalance in the antioxidant system can be discovered in diabetic induced renal failure tissues and a percentage of normal tissues, which can lead to endogenous formation of reactive oxygen species and cellular inability to cope with external peroxidative attacks. This study also shows that by exhibiting antioxidant and anti-hyperglycemic property the extract of manjishtha affords protection against the renal damage associated with diabetes.

Key words：

Chronic kidney disease, Oxidative stress, Antioxidants, Manjishtha

5

The therapeutic potential of Disintegrin ARGDRR in AKI to CKD continuum
去整合素 ARGDRR 在 AKI 到 CKD 連續體的療效潛力

Tsai-Chen Chiang[1], Jia-Huang Chen[1], Shao-Yu Yang[2], Jenq-Wen Huang[2], Kuan-Yu Hung[2], Tur-Fu Huang[4], Woei-Jer Chuang[5], Chih-Kang Chiang[1,2,3]

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Background: Acute kidney injury (AKI) can lead to progress renal fibrosis, resulting in chronic kidney disease (CKD) and end stage renal disease (ESRD). Nevertheless, the underlying pathological mechanisms remain unclear. Platelet activation has been demonstrated as one of the important factors involved in the pathophysiology of AKI, and studies show the therapeutic potential for using platelet inhibitors or antagonists in ischemia-reperfusion (IR)-induced AKI models. However, drug-induced side effects, including thrombotic microangiopathies (TMA)-related kidney damage, thrombocytopenia and bleeding, hinder clinical application in AKI or CKD treatment. Our newly developed dual effect disintegrin, ARGDRR, is derived from snake venom exert a high affinity to αIIbβ3 and αvβ3 binding affinity without causing bleeding and other thrombosis-related side effects.

Methods: We performed a unilateral ischemia-reperfusion injury (UIRI) model to investigate integrin αIIb(Itga2b) and β3(Itgb3) mRNA levels in the injured kidney for 15 days. For exploring the therapeutic efficiency of ARGDRR in AKI, we administered ARGDRR post-ischemic injury and measured platelet activation after 24 hours using quantitative polymerase chain reaction (qPCR) and immunohistochemistry (IHC) for Itgb3, Ngal, and CD42b. For exploring the therapeutic efficiency of ARGDRR in CKD progression, we administrated ARGDRR daily for 15 days after IRI with nephrectomy, and examined the difference of renal dysfunction, renal fibrosis, and cell death compared to sham group.

Results: We found that platelet activation with progressively increased mRNA level of platelet glycoprotein IIb-GPIIIa (Itga2b and Itgb3) in the uIRI kidney over time. After 24 hr of ischemic AKI, ARGDRR administration reduced Itgb3, Kim1 and Ngal mRNA level, indicating its efficacy in protecting the kidneys by inhibiting platelet activation and aggregation. In AKI to CKD transition, serum creatine and blood urea nitrogen (BUN) were significantly lower both in efficacious and high dose of ARGDRR administration group. Also, ARGDRR administration alleviated renal fibrosis, cell apoptosis and senescence-related molecules p21 and Ctgf expression in the AKI to CKD transition. Moreover, ARGDRR significantly reduced the expression of inflammatory cytokine, Il6 after ischemic AKI.

Conclusions: Our results have successfully proved our hypothesis that disintegrin-ARGDRR has the potential for renal protection in the transition of AKI to CKD through inhibition of platelet activation, anti-apoptosis and anti-inflammation during acute injury.

Keywords: acute kidney injury, chronic kidney disease, disintegrin, ARGDRR

6

The Correlation of Hypercholesterolemia and Kidney Damage Status on High-Fat Induced Rats (*Rattus Norvegicus*) after Intervention of Synbiotic Drink Containing *Lactobacillus sp.* Isolates

B Melvern[1], AN Yosanto [2], HA Sudiarto[1]

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Background:

Hypercholesterolemia may lead to renal damage due to the accumulation of cholesterol in kidneys, resulting oxidative damage, i.e. generating reactive oxygen and lipid peroxidation. One of the final products from lipid peroxidation in cells is malondialdehyde (MDA). Synbiotic have been proposed to reduce cholesterol through variety of mechanisms. This study aimed to assess the correlation between total serum cholesterol and kidney MDA levels after intervention of synbiotic drink of Kepel (*Stelechocarpus burahol*) with the addition of *Lactobacillus casei* and *Lactobacillus plantarum* isolates.

Method:

The study utilized post-test randomized control group design. Twenty-five rats were divided into five groups. After one-week acclimatization the normal group was fed by standard diet 20 grams/day, while the negative control group and interfered groups (P1, P2, P3) were fed by 20 grams of high-fat diet for four weeks. The lipid profiles were checked to ensure the negative control group and interfered groups contracted dyslipidemia prior to receiving synbiotic drink (P1=1.2, P2=1.8, and P3=2.4) mL/day for four weeks. At the end of the study, serum total cholesterol were measured and tissue samples from kidney were taken to determine the MDA levels.

Result:

The mean of total cholesterol (TC) of normal group 96.79 (±2.44), negative control group 210.21 (±3.79), P1 group 161.97 (±3.05), P2 group 136.46 (± 3.79), P3 group 119.01 (±3.89). MDA levels of normal group 2.23 (±0.28134), negative control group 9.546 (±0.39627), P1 group 5.31 (±0.19609), P2 group 3.672 (±0.29761), P3 group 2.95 (±0.35391). One-way ANOVA and post-hoc Bonferroni test showed significant differences of both serum TC and MDA level between all groups after given synbiotic drink with the p-value = 0.000 ($p<0.05$). Bivariate Pearson correlation coefficient showed positive correlation between total serum cholesterol and kidney MDA level ($r = 0.990$, p-value = 0.000).

Conclusion:

This study suggests that there were positive correlation between hypercholesterolemia and kidney damage status with significant linear relationship. Also, synbiotic drink containing *Lactobacillus sp.* isolates could improved the cholesterol and kidney damage status outcome.

Keywords :

Synbiotic Drink, Lactobacillus, Hypercholesterolemia, Kidney Damage Status

7

Inhibition of angiopoietin-2 mitigates kidney injury by attenuating inflammation
抑制第二型血管生成素可以減緩腎臟損傷及發炎

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Background：
Angiopoietin-2 (Angpt2), generally considered as a Tie-2 antagonist, destabilizes endothelial cells, and primes them to respond to exogenous stimuli. By antagonizing the Tie-2 survival signal, Angpt2 leads to endotheliall apoptosis and vascular regression. Our previous studies have demonstrated that Angpt2 inhibition through overexpression of Angp1 attenuates kidney fibrosis. We aim to decipher the mechanistic role of Angpt2 inhibition from the early to advanced stages of kidney injury.
Methods：
We used *Tg*(*UBC-Cre*^{ERT2});*Angpt2*$^{F/F}$ transgenic mice to achieve universal deletion of *Angpt2*. A 0.25% adenine diet induced tubulointerstitial injury in murine kidneys. Analyses were performed separately after 3 and 4 weeks.
Results：
We demonstrated that *Angpt2* deletion resulted in lower levels of BUN and creatinine at the third and forth weeks. The expression of *Col1a1, Col3a1, and Acta2* was significantly lower in the kidneys of *Angpt2* deletion. Furthermore, the expression of *Ccr2, Cx3cr1, Ccl17,* and *Adgre1* decreased markedly in *Angpt2* deletion. Immunofluorescence staining revealed a significant reduction in the accumulation of F4/80^{+} macrophages in *Angpt2* deletion 4 weeks after adenine-induced tubulointerstitial injury. The protective effect of Angpt2 deletion on the kidneys was further confirmed by a decrease in renal inflammation and tubulointerstitial injury at 4 weeks after the adenine diet. Flow cytometry demonstrated a significant decrease in the proportion of CD11b^{+} macrophages in *Angpt2* deletion. We observed a marked decrease in both the M1 and M2 subpopulations of macrophages, defined by Ly6c expression, in *Angpt2* deletion. Isolated CD11b^{+};CD140b^{-};CD324^{-};VEGFR2^{-};Ly6G^{-} macrophages from kidneys after 3-week adenine diet showed reduced expression of the pro-inflammatory genes *Ccl17, Ccl22,* and the anti-inflammatory gene *iNos* in *Angpt2* deletion. Finally, ex vivo μCT scanning revealed a significant reduction in adenine-induced microvascular rarefaction in *Angpt2* deletion 3 weeks after initiating the injury.
Conclusions：
Angpt2 deletion attenuates kidney injury in adeninine-induced tubulointerstitial damage. The protective effects may arise from reduced inflammation and preserve microvascular rarefaction. Therapeutic strategies targeting Angpt2 could be a convincing treatment for kidney injury.
Key words：
Angpiopoietin-2, kidney injury, inflammation, tubulointerstitial disease