



Oral Communications 7 Basic Research

December 6, 2025 (Saturday) 11:00~12:30

Venue : Room 7 (703)

Chair(s)

Jung Pyo Lee, Sheng-Wen Wu

11:00-11:09

Transcription Factor SREBF1 Regulating the Expression of Lipid Metabolism Gene FADS1 Participates in Lupus Nephritis Glomerular Mesangial Cells Injury
APCN20250292

Manrong He

Department of Nephrology, West China Hospital, Sichuan University

11:09-11:18

Mechanisms of Pathogenic Podocin Mutations in Nephrotic Syndrome Reveal Discrete Trafficking and Degradation Pathways
APCN20250094

Lu Pei-Chen

Bristol Renal, Translational Health Sciences, Bristol Medical School, University of Bristol

11:18-11:27

Bone-Heart Axis in Mild Chronic Kidney Disease—Mineral and Bone Disorder: Phosphate Metabolism and Tissue-Specific Remodeling
APCN20250960

EVDOKIA BOGDANOVA

Research Institute of Nephrology, Pavlov University

11:27-11:36

Deep shotgun metagenomic analysis of the oral microbiome identifies certain bacterial plasmids associated with IgA nephropathy
APCN20250227

Sho Hamaguchi

Department of Nephrology, Juntendo University Faculty of Medicine

11:36-11:45

CCN1 Regulates Macrophages in an ARG1-Dependent Manner to Promote Renal Tubular Epithelial Cell Proliferation in Ischemic Acute Kidney
APCN20250108

Ningxin Zhang

Department of Nephrology, the Affiliated Hospital of Qingdao University

11:45-11:54

Suppression of B Cell Activating Factor by Physalis angulata Extract in a Doxorubicin-Induced Rat Model of Nephrotic Syndrome: Exploring Its Role as Adjunctive Therapy
APCN20251090

Astrid Kristina Kardani

Division of Nephrology, Department of Pediatric, Dr. Saiful Anwar General Hospital, Faculty of Medicine, Brawijaya University





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|-------------|--|--|
| 11:54-12:03 | FHL2 as A Cofactor of RXR to Regulate FGF23 Expression in Chronic Kidney Disease APCN20250972 | Chih-Yuan Niu Division of Internal Medicine, Department of Nephrology, National Yang Ming Chiao Tung University |
| 12:03-12:12 | The Mineralocorticoid Receptor-TRPC5 Axis Drives Macrophage-Mediated Inflammation in Diabetic Kidney Disease APCN20250722 | Wada Masafumi Kawasaki medical school Department of Nephrology and Hypertension |
| 12:12-12:21 | Study on The Mechanism of A Novel Kidney Protective Protein TMEM52B Alleviating Renal Fibrosis by Upregulating MYDGF APCN20250390 | XUE Rui Department of Nephrology, The First Affiliated Hospital of Shenzhen University, Shenzhen Second People's Hospital |
| 12:21-12:30 | The Protective Role of Aldo-Keto Reductase Family 1 Member A1 in Kidney Allograft: Beyond S-Nitrosylation APCN20250559 | Weng, Shuo-Chun Geriatrics and Gerontology Research Center, College of Medicine, National Chung Hsing University |



Oral Communications : Basic Research
Abstract Submission No. : APCN20250292

Transcription Factor SREBF1 Regulating the Expression of Lipid Metabolism Gene FADS1 Participates in Lupus Nephritis Glomerular Mesangial Cells Injury

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Abstract

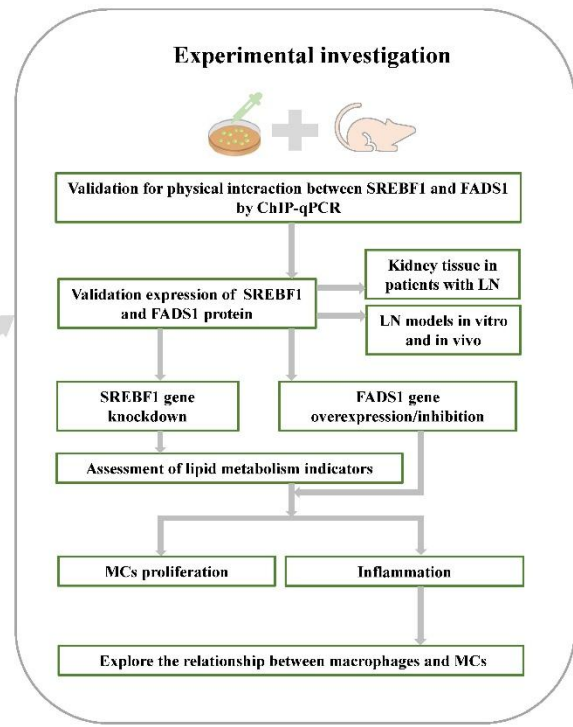
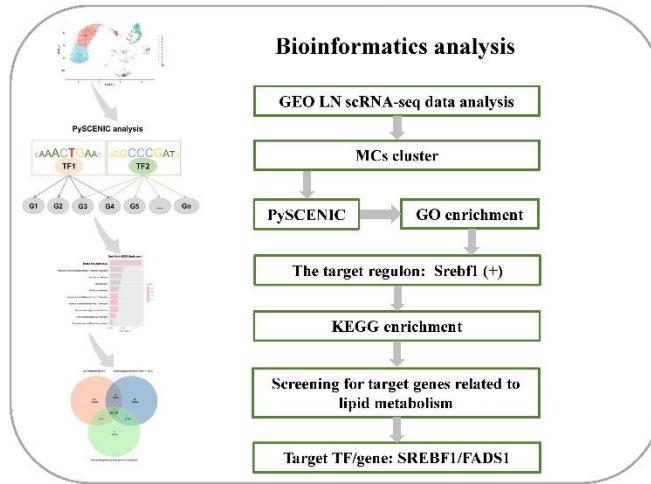
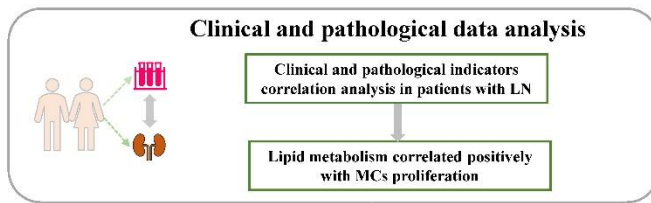
Background: Mesangial cells (MCs) injury is a key feature of lupus nephritis (LN). Elevated lipid levels were associated with LN prognosis in previous reports; however, the association between MCs and lipid metabolism remains unclear. This study aims to identify lipid metabolism-related transcription factors (TFs) and their target genes in MC injury in LN.

Methods: Correlations between LN clinical and renal pathological indicators were evaluated. Public single-cell RNA sequencing data from LN mouse kidneys were analyzed to identify lipid metabolism-related regulons, TFs, and their downstream target genes in the MCs cluster. TF-target gene expression and physical interaction were validated by immunohistochemistry and chromatin immunoprecipitation-qPCR (ChIP-qPCR). In vitro and in vivo experiments were conducted to examine their roles in MCs inflammation and proliferation.

Results: Clinical and renal pathological data of 289 LN patients indicated that elevated lipid levels are positively correlated with MCs proliferation. The most upregulated regulon, Srebf1(+), and its downstream lipid metabolism-related gene, Fads1, were identified. SREBF1 directly bound to the FADS1 promoter. Both SREBF1 and FADS1 were upregulated in LN models. Inhibition of SREBF1 improved lipid metabolism and reduced MCs injury. FADS1 overexpression confirmed the contribution of the SREBF1/FADS1 axis to inflammation and proliferation. Moreover, supernatants from M1 macrophages increased SREBF1 expression in MCs, highlighting macrophage-MC cross-talk in lipid-inflammatory regulation.

Conclusion: In LN, elevated lipid levels are positively correlated with MCs proliferation. The lipid metabolism-related SREBF1/FADS1 contributes to MCs injury, and its inhibition may alleviate MCs inflammation and proliferation.

Keywords : lupus nephritis; single-cell RNA sequencing; transcriptional factor; mesangial cells; lipid metabolism



Oral Communications : Basic Research
Abstract Submission No. : APCN20250094

Mechanisms of pathogenic podocin mutations in nephrotic syndrome reveal discrete trafficking and degradation pathways

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Abstract

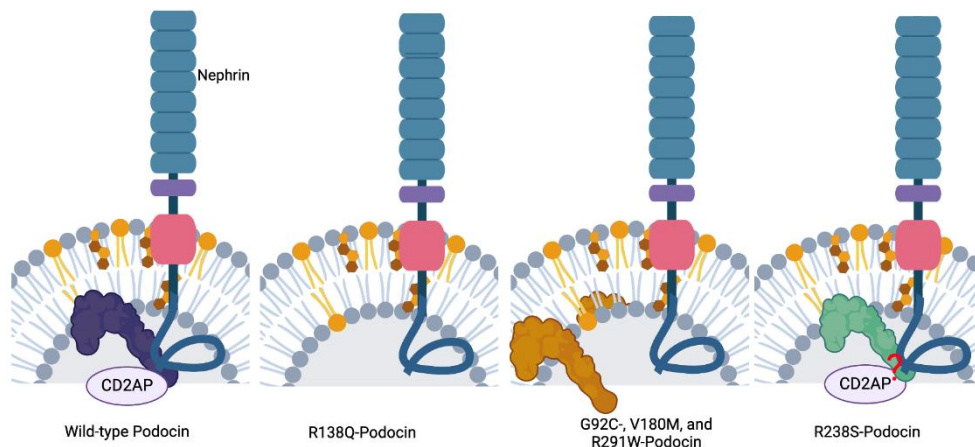
Nephrotic syndrome is frequently linked to mutations in podocin (NPHS2), notably the severe R138Q variant. Using immortalized human podocytes and lentiviral transduction, we introduced Myc-tagged podocin mutants (G92C, V180M, R138Q, R238S, and R291W) to investigate their pathogenic mechanisms. Proteasome inhibition (MG132) rescued R138Q-Podocin, enabling its plasma membrane (PM) and detergent-resistant microdomain (DRM) localization, highlighting its therapeutic potential.

Distinct mutations exhibited various effects: G92C, V180M, and R291W reduced PM localization and DRM distribution, whereas R238S increased DRM distribution despite PM mislocalization. Proteomic analysis revealed that wild-type (WT) podocin interacts with proteins involved in endocytosis, adhesion, and signalling, whereas R138Q-Podocin is associated with ER quality control and proteasomal degradation. Myosin VI was identified as a novel podocin-binding partner, suggesting a role in podocin trafficking.

These findings highlight the diverse pathogenic mechanisms of podocin mutations and underscore mutation-specific therapeutic strategies, particularly for R138Q, that target degradation, trafficking, and membrane microdomain distribution.

Keywords : genetic disease, kidney, podocin, nephrotic syndrome, gene mutation

Diverse Pathogenic Mechanisms of Podocin Mutants



Oral Communications : Basic Research

Abstract Submission No. : APCN20250960

Bone-Heart Axis in Mild Chronic Kidney Disease—Mineral and Bone Disorder: Phosphate Metabolism and Tissue-Specific Remodeling

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Abstract

Introduction: In our previous study of a CKD-MBD cohort (N=1,213; CKD stages 1-5; 48% male; age 48±16 years), serum phosphate (Pi) levels were independently associated with echocardiographic signs of left ventricular hypertrophy, even in early-stage CKD. To investigate the mechanistic basis of Pi-mediated cardiovascular remodeling in mild CKD-MBD, we conducted a translational study combining experimental and clinical approaches.

Methods: Experimental CKD was induced in adult male spontaneously hypertensive rats (SHRs) by 3/4 nephrectomy (Nx) with a 4-month follow-up; sham-operated SHRs (SO) were controls. Animals received standard chow (0.6% phosphorus). We assessed: renal function (serum creatinine, proteinuria, interstitial fibrosis); cardiovascular parameters (systolic blood pressure, myocardial mass index); phosphate metabolism (serum Pi, renal Pi excretion indices, PTH, FGF23); tissue analysis (myocardial/bone phosphorus, myocardial/bone histomorphometry); molecular pathways: Slc20a1 (PiT1), Slc20a2 (PiT2), Mapk3/1, phospho-ERK1/2 (RT-qPCR, Western blot, IHC with quantitative morphometry, confocal microscopy). Clinical study enrolled 78 patients with biopsy-proven immune glomerulopathies (CKD S1-4; 52% male; age 43 ± 13), excluding extrarenal diseases and immunosuppressive therapy. Control group: healthy subjects of corresponding age and gender (n=10). Evaluations included: cardiac function (echocardiography, NT-proBNP); phosphate metabolism (serum Pi, renal Pi excretion indices, 25OHD, PTH, FGF23, Klotho); bone turnover (osteocalcin, bone/total ALP, β-CrossLaps).

Results: Nx rats exhibited features of human CKD S2 with lower bone turnover (↓osteoblasts, osteocytes numbers, eroded perimeter, Figure 1A). Serum Pi, myocardial P content were higher in the Nx group vs SO, without significant differences in 24-hour urinary Pi excretion, bone P content, PTH, FGF23 (Figure 1A-B). In CKD-MBD, bone Slc20a1 and Mapk1 expression were lower (Figure 1D) with a reduction in PiT1 and phospho-ERK1/2 IHC staining (Figure 1E). Myocardial P accumulation, fibrosis, cardiomyocyte hypertrophy in Nx (Figure 1C) accompanied with higher Slc20a2 and Mapk3 mRNA, PiT2 protein, phosphorylated ERK1/2 expressions (Figure 1F,G). In clinical study Pi and FEPI were independently associated with echocardiographic parameters of cardiac remodeling. Mild CKD already have elevated LVMI with lower 25OHD3 and osteocalcin (Figure 1H,I,J), suggesting osteoblast suppression with defective mineralization in this group. Moderate to severe CKD showed obvious cardiac remodeling (Figure 1H) with mineral disturbances – higher PTH, β-CrossLaps, BAP, and persistent low 25OHD and osteocalcin.

Conclusion: Bone and myocardial responses to phosphate retention manifest early in both experimental and clinical mild CKD-MBD. Experimental data implicate myocardial remodeling in mild

Oral Communications : Basic Research

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Deep shotgun metagenomic analysis of the oral microbiome identifies certain bacterial plasmids associated with IgA nephropathy

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Abstract

Introduction: Exogenous antigens have been implicated in the pathogenesis of IgA nephropathy (IgAN), and our recent studies have demonstrated that antigenic stimulation of the upper respiratory mucosa induces the production of nephritogenic IgA antibodies. Although several previous studies have examined the oral microbiome in IgAN patients, most have relied on 16S rRNA sequencing and lacked species-level resolution or analysis of mobile genetic elements associated with individual bacteria. Therefore, this study aimed to comprehensively analyze the oral microbiome of IgAN patients by performing deep shotgun metagenomic sequencing and to identify microorganisms associated with the disease pathogenesis.

Methods: Saliva samples were collected from 44 patients with IgAN, 25 with chronic tonsillitis, and 11 healthy individuals. Shotgun sequencing was performed on extracted DNA. Universal single copy marker genes present in 150 base pairs short reads were used to analyze bacterial species and their relative abundances. Additionally, de novo assembly of short reads was conducted to generate contigs ranging from several thousands to tens of thousands of base pairs. The generated contigs were classified into three categories—chromosome, plasmid, and phage—based on their genomic features. Subsequently, the diversity and abundance of the contigs were compared among categories.

Results: Shotgun sequencing yielded an average of 56 million paired-end short reads per sample. Analysis of bacterial species identified few bacterial species were consistently enriched in IgAN patients compared to the other groups. However, contig-based analysis revealed that only plasmid contigs exhibited significant differences in beta diversity. Among these plasmid contigs, specific bacterial plasmids were significantly increased in IgAN patients compared to the other groups (Fig.1). Interestingly, the identified plasmids showed a greater increase in IgAN patients compared to their host bacteria. To validate this finding, the host bacterial strain was isolated from the saliva of IgAN patients and healthy individuals. Subsequent long-read sequencing confirmed that only the strain which was isolated from IgAN patients harbored a plasmid. Finally, comparative genome analysis showed that the plasmid was significantly abundant in IgAN patients.

Conclusion: Through deep shotgun metagenomic sequencing and analysis using de novo assembly, it was revealed that specific bacterial plasmids were significantly increased in the oral cavity of IgA nephropathy patients. While previous studies on disease-associated microbiomes have primarily focused on the relationship between bacterial species and disease, our findings suggest that plasmids, as mobile genetic elements within the commensal microbiome, may play a critical role in the pathogenesis of IgAN.

Keywords : IgA nephropathy, metagenomic analysis, mobile genetic elements

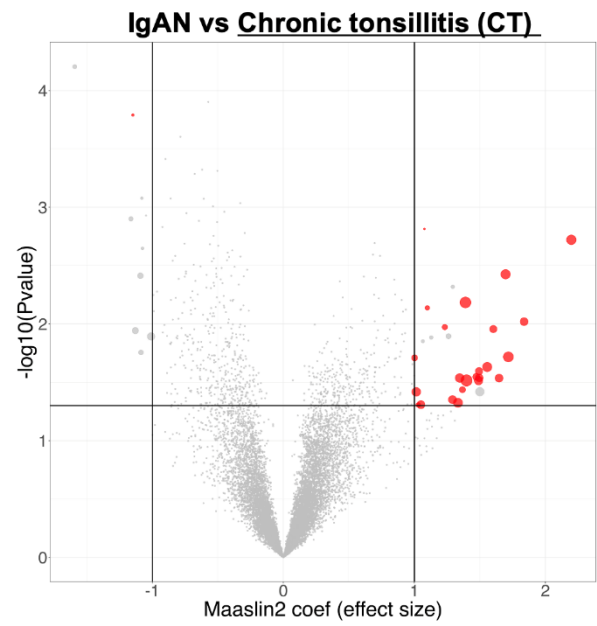
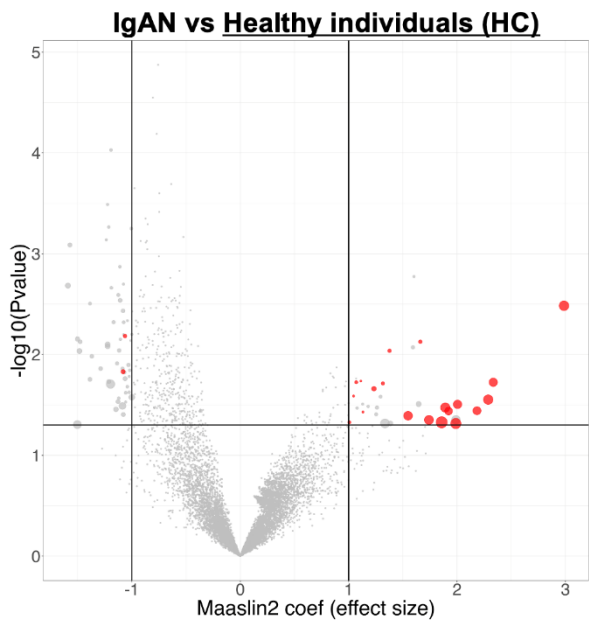


Fig.1
 Volcano plots show plasmid contigs; those significantly enriched in IgAN patients appear in the upper-right. Most enriched plasmids originate from a single bacterial genus (red dots).

CCN1 Regulates Macrophages in an ARG1-dependent manner to Promote Renal Tubular Epithelial Cell Proliferation in Ischemic Acute Kidney

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Abstract

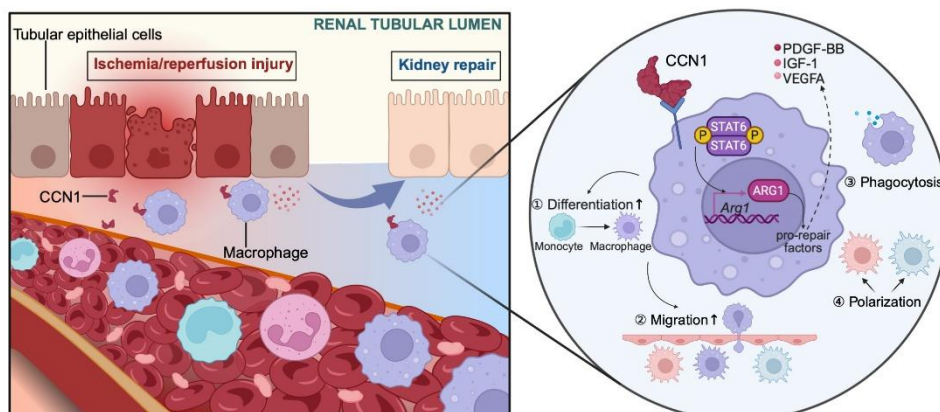
Introduction: The mechanisms underlying injury and repair following acute kidney injury (AKI) remain incompletely understood, with macrophages playing critical roles in this process. CCN1, a secreted matricellular protein, has been identified as an early biomarker of AKI. However, the specific role of CCN1 in modulating macrophage function during AKI is still unclear.

Methods: This study investigated the expression dynamics of CCN1 and its relationship with macrophages in AKI using a contralateral nephrectomy followed by unilateral ischemia-reperfusion injury (I/R) mice model. Bone marrow-derived macrophages (BMDMs) were isolated to evaluate the effects of CCN1 on the differentiation, migration and related functions of macrophages by flow cytometry, quantitative PCR, scratch assay, and transwell migration assay, etc. A co-culture system of BMDMs and renal tubular epithelial cells (HK-2) were used to assess the effect of CCN1 on macrophage-mediated proliferation of tubular epithelial cell. Furthermore, RNA-seq and deconvolution analysis by using BayesPrism model were employed to elucidate the molecular mechanisms by which CCN1 modulates macrophages, followed by targeted in vitro validation experiments.

Results: CCN1 expression was significantly upregulated in renal tubular epithelial cells and was closely localized to infiltrating F4/80⁺ macrophages following I/R-AKI. In vitro experiments demonstrated that HK-2 cells exhibited elevated CCN1 expression and secretion upon injury stimulation. Meanwhile, CCN1 protein promoted macrophage differentiation and migration, and enhanced macrophage-mediated tubular epithelial cell proliferation. RNA-seq and deconvolution revealed that CCN1 facilitated the proportion of pro-repairing macrophages, potentially through promoting the expansion of Arg1^{hi} macrophage subsets. Further in vitro experiments confirmed the increase of Arg1^{hi} macrophage after CCN1 treatment, while experiments using an ARG1 inhibitor further substantiated that CCN1 enhances renal tubular epithelial cell proliferation in an ARG1-dependent manner.

Conclusion: In I/R-induced AKI, tubular epithelial cells significantly increase CCN1 expression and secretion, which promotes macrophage differentiation and migration and enhancing tubular epithelial cell proliferation in an ARG1-dependent manner, facilitating renal repair. These findings could lead to the identification of potential therapeutic targets for the treatment of ischemic acute kidney injury.

Keywords : acute kidney injury, macrophage, Arginase-1, metabolic reprogramming, CCN1



Oral Communications : Basic Research

Abstract Submission No. : APCN20251090

Suppression of B Cell Activating Factor by *Physalis angulata* Extract in a Doxorubicin-Induced Rat Model of Nephrotic Syndrome: Exploring Its Role as Adjunctive Therapy

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Abstract

Background: Nephrotic syndrome (NS) in children remains a major clinical challenge in Indonesia, particularly due to its frequent relapses and dependence on long-term corticosteroid therapy. Although steroids are effective in inducing remission, prolonged use can result in significant side effects. B Cell Activating Factor (BAFF), a cytokine critical for B cell survival and activation, has been implicated in podocyte injury and disease progression in NS. *Physalis angulata*, a medicinal plant abundant in Indonesia, contains phytosteroids known for their anti-inflammatory and immunomodulatory properties. However, its role in modulating BAFF levels in nephrotic syndrome has not been well explored.

Objective: This study aimed to assess the effect of *Physalis angulata* extract on BAFF levels in the serum and kidney tissues of rats with doxorubicin-induced nephrotic syndrome.

Methods: Nephrotic syndrome was induced in male Sprague-Dawley rats via a single tail vein injection of doxorubicin at 7 mg/kg. A total of 36 rats were divided into nine groups: healthy control, nephrotic model, prednisone-treated group, three groups receiving *Physalis angulata* extract at doses of 500, 1500, or 2500 mg/kg, and three additional groups receiving combined treatment of prednisone with each dose of extract. Serum BAFF concentrations were measured using ELISA, and BAFF expression in renal tissues was evaluated through immunofluorescence staining, quantified with ImageJ software. Statistical analysis was performed to determine differences between groups.

Results: The nephrotic control group exhibited significantly elevated serum and renal BAFF levels, indicating immune dysregulation and podocyte injury. Treatment with *Physalis angulata* extract, especially at 1500 and 2500 mg/kg in combination with prednisone, significantly reduced both serum and kidney BAFF expression ($p < 0.05$), suggesting an enhanced immunomodulatory effect. A strong positive correlation was observed between serum and renal BAFF expression levels. Notably, the group receiving 2500 mg/kg of extract combined with prednisone showed the most pronounced reduction, approaching levels observed in the healthy control group. This dose-dependent response highlights the therapeutic potential of *Physalis angulata* as an adjunct to standard steroid therapy.

Conclusion: *Physalis angulata* extract demonstrated the potential to lower BAFF levels in serum and suppress its expression in kidney tissues of rats with nephrotic syndrome. These findings support its role as a promising adjunctive therapy and warrant further investigation into its clinical applicability and long-term safety profile.

Keywords : Nephrotic syndrome, BAFF, *Physalis angulata*, doxorubicin-induced Rat model

Oral Communications : Basic Research
Abstract Submission No. : APCN20250972

FHL2 as a cofactor of RXR to regulate FGF23 expression in chronic kidney disease

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Abstract

Mineral and bone disorder (MBD) is a common complication in individuals with chronic kidney disease (CKD), which leads to secondary hyperparathyroidism, renal osteodystrophy, vascular calcification and uremic cardiomyopathy. These conditions are associated with increased risk of fracture and substantial cardiovascular morbidity and mortality. Fibroblast growth factor 23 (FGF23) plays a key role in the pathogenesis of CKD-MBD. 1,25-dihydroxyvitamin D is an important regulator of FGF-23 expression, acting through the vitamin D receptor (VDR) and vitamin D responsive elements (VDRE), with a key transcription factor called retinoid-X receptor (RXR). However, RXR could not be targeted for therapy since its essential role in cardiac morphogenesis. The goal of this study was to discover a RXR cofactor that is abundant in osteoblast and examine its potential as a target for therapy.

We employed transcriptomic analysis of human data and an animal reporter system to pinpoint four LIM domains 2 (FHL2) as a potential target. We investigated the mRNA and protein expression patterns of FHL2 in the bone, vessel and myocardium of both human and animal subjects with CKD. To examine the role of FHL2 in the RXR transcription machinery, we conducted coimmunoprecipitation and chromatin immunoprecipitation experiments. Next, we manipulated FHL2 expression in cultured osteoblast to examine its impact on FGF23 production. Finally, we employed FHL2 -null mice to confirm the role of FHL2 in the regulation of FGF-23 expression and effects on cardiovascular system and bone health.

In the context of CKD subjects, FHL2 interacts structurally and functionally with RXR, acting as a coactivator of RXR. Notably, the inhibition of FHL2 expression averts FGF23 expression and mitigates vascular calcification and cardiac hypertrophy in CKD animals, without causing detrimental effects on the skeletal system. These observations provide evidence that FHL2 is a promising target for FGF23 upregulation and thus treating MBD in patients with CKD.

Keywords : chronic kidney disease (CKD), mineral and bone disorder (MBD), fibroblast growth factor 23 (FGF23), retinoid-X receptor (RXR), FHL2

Oral Communications : Basic Research

Abstract Submission No. : APCN20250722

The Mineralocorticoid Receptor–TRPC5 Axis Drives Macrophage-Mediated Inflammation in Diabetic Kidney Disease

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Abstract

Background: Diabetic kidney disease (DKD) is a leading cause of end-stage renal disease (ESRD). Although DKD is characterized by a low-renin state that limits aldosterone-driven mineralocorticoid receptor (MR) activation, aldosterone-independent MR activation occurs under conditions like diabetes and obesity, contributing to renal damage. Recent trials (FIGARO-DKD and FIDELIO-DKD) have shown that the non-steroidal MR antagonist finerenone provides renoprotection, supporting its use in DKD. However, the anti-inflammatory mechanisms remain unclear. Our previous studies showed that MR activation promotes inflammasome activity in macrophages. TRPC channels, particularly TRPC5, may regulate Ca²⁺ influx and modulate inflammatory responses. This study investigates the MR–TRPC pathway's role in inflammasome activation using a progressive DKD mouse model (eNOS-db/db).

Methods: All mice background is C57BL/6. eNOS-KO db/db mice were generated by crossing endothelial nitric oxide synthase knockout (eNOS-KO) mice with type 2 diabetic db/db mice. We randomized into three groups, WT, eNOS-KO db/db with vehicle and eNOS-KO db/db with Finerenone. eNOS-KO db/db were treated with Finerenone for 4 weeks from 8 weeks of age in eNOS-KO db/db with Finerenone group. All mice sacrificed at 12 weeks of age. Macrophage infiltration was examined via F4/80 immunofluorescence staining and qPCR. Fibrosis was evaluated by Masson's trichrome staining, collagen IV staining, and qPCR analysis of fibrosis-related genes (TGFβ, CTGF, fibronectin). To investigate the relationship between MR activation and macrophage-mediated inflammation, we conducted in vitro assays using bone marrow–derived macrophages (BMDMs).

Results: Administration of finerenone significantly reduced albuminuria in eNOS-db/db mice compared to the eNOS-KO db/db vehicle-treated group. Increased infiltration of macrophages, as detected by F4/80 immunostaining, was observed in the kidneys of eNOS-db/db mice relative to control mice. Finerenone treatment markedly attenuated this macrophage infiltration. In BMDMs cultured in aldosterone-containing media, finerenone suppressed LPS-induced secretion of IL-6 to supernatant. Aldosterone stimulation led to an upregulation of TRPC5 protein expression in BMDMs. Notably, inhibition of TRPC5, but not TRPC6, completely abolished LPS-induced IL-6 expression and secretion. Furthermore, LPS stimulation triggered a calcium (Ca²⁺) influx in BMDMs, which was effectively suppressed by TRPC5 inhibition. These findings suggest that the aldosterone–MR–TRPC5 signaling axis contributes to inflammatory responses in macrophages, potentially via the NF-κB pathway.

Conclusion: Our study suggests that the renal protective effects of finerenone are at least partly mediated by suppression of chronic inflammation. We revealed that the MR–TRPC5 axis in macrophage has a pivotal role of maintainof chronic inflammation in kidney diseases.

Keywords : DKD(Diabetic Kidney Disease), Finerenone

Oral Communications : Basic Research
Abstract Submission No. : APCN20250390

Study on the mechanism of a novel kidney protective protein TMEM52B alleviating renal fibrosis by upregulating MYDGF

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Abstract

Background: Renal tubulointerstitial fibrosis is a central pathological process contributing to kidney dysfunction and progression to end-stage renal disease. Through exome sequencing across human tissues, transmembrane protein 52B (TMEM52B) was identified as highly expressed in the kidney, suggesting its potential role in renal function and injury. This study investigates TMEM52B's function and underlying mechanisms in tubular injury and renal fibrosis.

Methods: Using CRISPR-Cas9 and Cre-lox systems, we generated both systemic and tubule-specific TMEM52B knockout mice on a C57BL/6 background. Unilateral ureteral obstruction (UUO) surgery was performed to induce renal injury and fibrosis. We assessed pathological changes post-knockout and conducted in vitro experiments to elucidate TMEM52B's molecular role.

Results: TMEM52B expression was absent in knockout mice and significantly reduced in UUO-induced kidneys. Histological and immunofluorescence analyses revealed that TMEM52B-deficient mice exhibited more severe tubular injury and fibrosis following UUO. qPCR and IHC confirmed increased fibrosis markers in knockout mice. Proteomic analysis showed a significant reduction in Myeloid-Derived Growth Factor (MYDGF) in UUO kidneys, with further decline in TMEM52B knockout UUO mice. In vitro, TGF- β 1 stimulation reduced TMEM52B expression in mouse tubular C1.1 cells, and TMEM52B modulation directly affected MYDGF levels.

Conclusion: TMEM52B loss exacerbates renal tubular damage and fibrosis, potentially via MYDGF regulation. Targeting TMEM52B could offer a new therapeutic avenue to prevent or slow kidney disease progression.

Keywords : Renal tubulointerstitial fibrosis; Tubular injury; TMEM52B

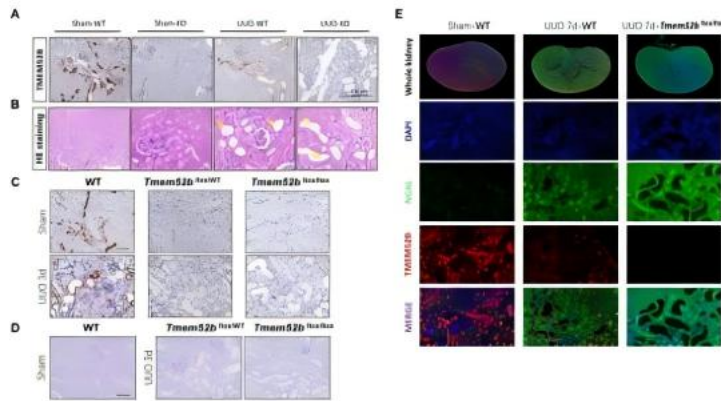


Figure 1. TMEM52B expression is negatively correlated with tubular injury in kidney from TMEM52B knockout mice with 3-days UO injury. Representative IHC staining of TMEM52B from (A) TMEM52B system knockout mice and (C) TMEM52B tubule-specific knockout mice with 3-days UO injury; (B) Representative HE staining from TMEM52B system knockout mice with 3-days UO injury; (D) Representative PAS staining from TMEM52B tubule-specific knockout mice with 3-days UO injury. (E) Representative Immunofluorescence staining from TMEM52B tubule-specific knockout mice with 3-days UO injury. Blue: DAPI; Green: NG2; Red: TMEM52B. Sham: faked surgical intervention; UO: unilateral ureteral obstruction; WT: Wide Type; KO: TMEM52B knockout; WT¹: Tmem52b flox/flox Ksp Cre^{-/-}; Tmem52b flox/WT: Tmem52b flox/WT Ksp Cre^{+/-}; Tmem52b flox/flox: Tmem52b flox/flox Ksp Cre^{+/-}. Scale bar=100 μ m.

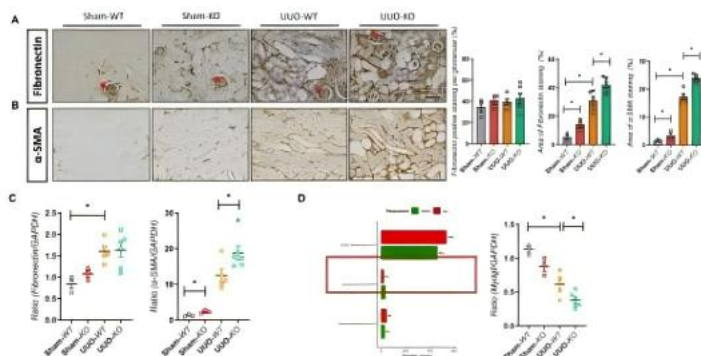


Figure 2. TMEM52B knockout in the kidney aggravated tubulointerstitial fibrosis through regulation of MYDGF from TMEM52B system knockout mice with 3-days UO injury. Representative IHC staining of (A) Fibronectin and (B) α -SMA from TMEM52B system knockout mice with 3-days UO injury; (C) Quantitative real-time PCR shows the relative expression of Fibronectin and α -SMA from TMEM52B system knockout mice with 3-days UO injury; (D) Through proteomic analysis, a total of 62 proteins with significant differences (greater than or equal to 1.5 times) were screened between the WT and KO groups under the UO model, among which the difference in MYDGF decrease was the most significant, and was further verified by quantitative real-time PCR; UO: unilateral ureteral obstruction; WT: Wide Type; KO: TMEM52B knockout. Scale bar=100 μ m.

Oral Communications : Basic Research
Abstract Submission No. : APCN20250559

The Protective Role of Aldo-Keto Reductase Family 1 Member A1 in Kidney Allograft: Beyond S-Nitrosylation

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Abstract

Background: Aldo-keto reductase family 1 member A1 (Akr1A1) is a NADPH-dependent glycolytic enzyme that catalyzes the reduction of aldehydes to their corresponding alcohols. This study aimed to elucidate the role of Akr1A1 in protecting kidney allografts and to investigate the underlying molecular mechanisms.

Methods: A total of 40 human kidney allograft tissues and corresponding serum samples were analyzed using Banff classification, alongside assessment of short- and long-term clinical outcomes. Murine models of acute cellular rejection (ACR) were established in conjunction with unilateral renal artery ischemia-reperfusion injury (IRI) to mimic transplant-related stress. Akr1A1 knockout mice and ischemia-reperfusion cell models were employed to evaluate the role of CHOP and the Akr1A1/SIRT1/PGC-1 α pathway.

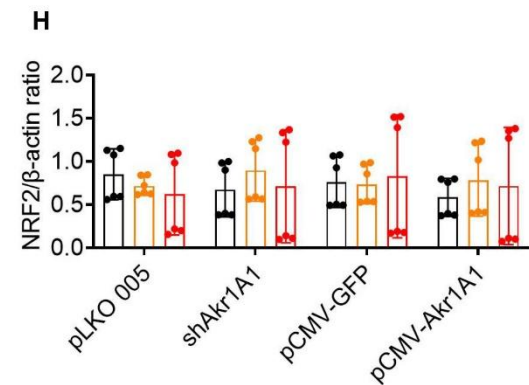
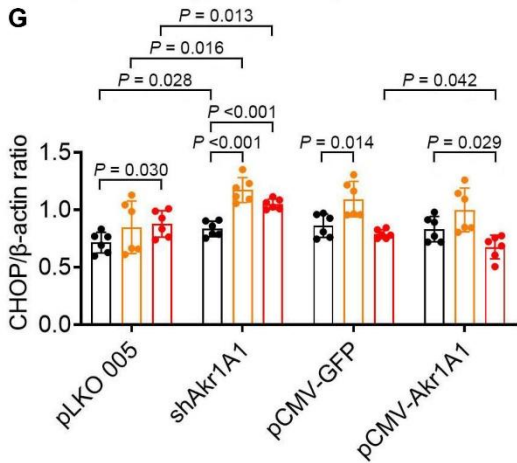
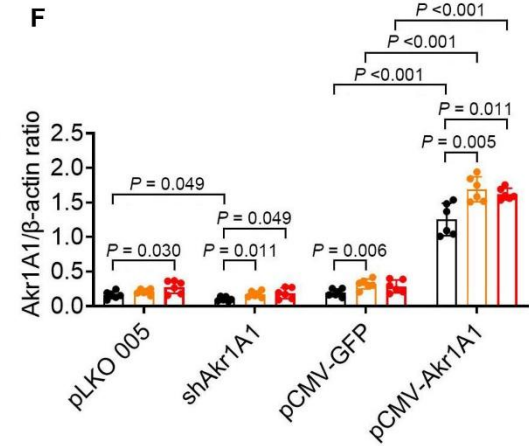
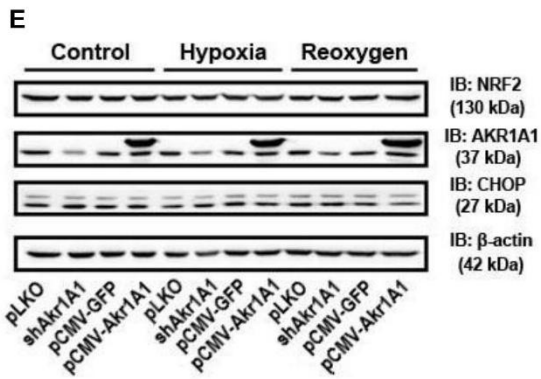
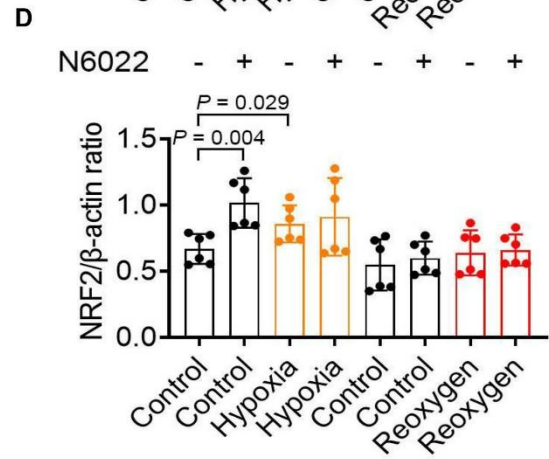
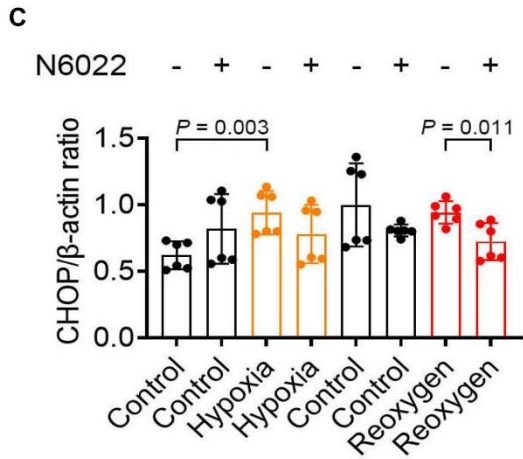
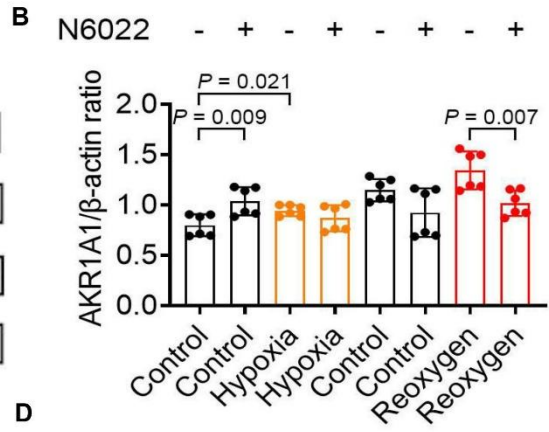
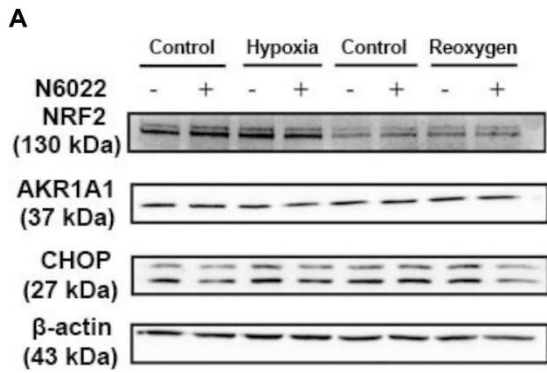
Results: In human samples, elevated expression of AKR1A1 in renal tubular cells was associated with tubular injury and oxidative stress, particularly in cases of rejection and acute tubular injury. Although an inverse correlation between AKR1A1 and pyruvate kinase isoenzyme M2 (PKM2) was observed, this relationship appeared non-specific. Increased AKR1A1 expression correlated with heightened oxidative stress but higher graft survival.

In vitro, hypoxia/reoxygenation (H/R) reduced cell viability and increased the expression of Akr1A1 and CHOP, a pro-apoptotic marker. Treatment with N6022, a GSNOR inhibitor that reduces protein S-nitrosylation, suppressed Akr1A1 activity and further increased cell viability under H/R, suggesting that reduced Akr1A1 activity alone does not directly drive CHOP expression. N6022 also elevated NRF2 levels, indicating exacerbated oxidative stress.

Genetic modulation experiments demonstrated that CHOP expression was upregulated in Akr1A1 knockdown cells (shAkr1A1) and downregulated in Akr1A1-overexpressing cells (pCMV-Akr1A1), supporting a direct role for Akr1A1 in regulating apoptosis-related gene expression. Additionally, a reciprocal relationship was observed between Akr1A1 and the SIRT1/PGC-1 α axis.

Conclusions: Our findings demonstrate that S-nitrosylation and the activation of the SIRT1/PGC-1 α signaling pathway play protective roles under conditions of Akr1A1 insufficiency. These pathways may represent compensatory mechanisms against oxidative stress and apoptosis in kidney allografts, providing potential therapeutic targets for improving transplant outcomes.

Keywords : Silent mating type information regulation 2 homolog 1 (SIRT1), Peroxisome-proliferator-activated receptor γ coactivator-1 α (PGC-1 α), kidney allograft injury, aldo-keto reductase, S-nitrosylation



• Control • Hypoxia • H/R