Introduction: We present a case of focal segmental glomerulosclerosis (FSGS) and acute-onset chronic inflammatory demyelinating polyneuropathy (CIDP) associated with rare neurofascin autoantibodies, supporting a newly defined neuro-renal syndrome.

Methods: A 48-year-old African-American male presented to the hospital with lower extremity paresthesias that progressed rapidly to bilateral upper and lower extremity weakness with areflexia. He underwent an electrodiagnostic study that demonstrated sural sparing, absent F waves, conduction block and markedly reduced recruitment of normal appearing motor unit potentials, consistent with acute inflammatory demyelinating polyneuropathy (AIDP) and received 2 g/kg of intravenous immunoglobulin. He also developed new-onset proteinuria with 10 gm on spot urine albumin/creatinine ratio (UACR). Urine microscopy revealed 10-20 RBCs/HFP with few dysmorphic RBCs and a fine granular cast. A limited kidney biopsy with 3 glomeruli without tubulointerstitial damage on light microscopy (LM) and severe podocyte foot process effacement on electron microscopy (EM) was interpreted as minimal change disease (MCD). He was started on 1mg/kg prednisone daily; however, subsequently developed respiratory failure due to neuromuscular weakness requiring mechanical ventilation and was treated with plasmapheresis for 7 sessions. The patient was later extubated and discharged to acute rehabilitation. He was readmitted 2 weeks later for a suspected AIDP relapse with respiratory failure, again prompting intubation and plasmapheresis for 5 sessions. Proteinuria worsened to 24 gm despite continued treatment with prednisone. A repeat kidney biopsy showed 1/12 glomeruli with segmental sclerosis and acute tubular damage on LM, no deposits on immunofluorescence and severe podocyte foot processes effacement on EM, resulting in a new diagnosis of primary FSGS. In light of waxing and waning symptoms and protracted course he was diagnosed with acute-onset CIDP. A detailed work up returned positive for NF antibodies, NF140 and NF155, that have been reported with IVIG-refractory acute-onset CIDP. He was treated with pulse dose IV methylprednisolone and tacrolimus resulting in marked improvement of both proteinuria of 100 mg and polyneuropathy over 6 months of follow up.

Results: FSGS and CIDP may share immunopathogenic mechanisms. NF is a protein encoded by Nfasc gene and belongs to the L1 family of immunoglobulin cell adhesion molecules that are involved in neuronal growth and development. NF is a paronal protein, critical to neuronal transmission. Interestingly, NF is also a part of podocyte cytoskeleton. The presence of NF antibodies and concurrence of severe proteinuria and polynuropathy suggests a strong neuro-renal interface. NF antibodies are typically of the IgG4 subclass.

Conclusions: Physicians should have a high clinical suspicion for sampling errors on kidney biopsy if the disease in question does not seem to respond to adequate treatment. Our patient was first diagnosed with MCD and AIDP; however, despite adequate treatment suffered a relapse and was later diagnosed with FSGS and a rare subtype of CIDP. The pathophysiological role NF 140 and NF 155 antibodies in FSGS and their prognostic significance needs validation in further studies.

SUN-002
INSERTIONS AND DELETIONS (INDELS) IN THE NON-TRANSLATED HUMAN GENOME UPSTREAM OF ZHX2 ALTER ZHX2 MRNA EXPRESSION IN MCD AND FSGS

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Introduction: We identified 5 InDels (size range 6 to 67) shared by than one patient and 40 others (size range 4 to 133) present in a single patient. These InDels were absent in controls and the 1000 genomes project. Patients with MCD and FSGS tip lesion had a high percentage of deletions (approximately 80%), whereas those with other forms of FSGS had mostly insertions (approximately 66%). Significance of these indels was verified by inserting one of these indels upstream of ZHX2 in single cell derived immortalized human podocytes by CRISPR-Cas9 approach. Podocytes carrying this InDel developed reduced ZHX2 expression.

Conclusions: Insertions and deletions upstream of the ZHX2 gene are commonly present in patients with MCD and FSGS patients and alter ZHX2 mRNA expression.

SUN-003
MECHANISM OF SELECTIVE ALBUMINURIA IN MINIMAL CHANGE NEPHROTIC SYNDROME

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Introduction: Water and electrolytes are filtered through slit membranes, however, in minimal change nephrotic syndrome with foot process effacement it is not well understood whether albumin molecules will be filtered through the slit membrane. We reported that albumin endocytosis by FcRn was enhanced in the podocyte of puromycin aminonucleoside (PAN)-induced minimal change nephrotic syndrome rat, and treatment with anti-FcRn antibody decreased albumin endocytosis and urinary protein (Kidney Int 2011).

Methods: Minimal change nephrotic syndrome model was induced by puromycin amino nucleoside, and podocytes were observed by electron microscope and low vacuum scanning electron microscope.

Results: Electron microscopy demonstrated many vesicles were observed in the podocytes of PAN rat with 3D observation. SDS-polyacrylamide electrophoresis of glomerular proteins isolated from PAN rats showed that several protein bands were increased than those from control rats, and those increased protein bands were identified as dynein -l, myosin 7 and myosin 9 by mass spectrometry. These motor molecules are capable of transporting vesicles containing albumin in the podocytes of PAN nephrotic rat. In renal biopsy, electron microscopic examination of human minimal change disease cases showed numerous vesicles and microtubules in podocytes, and a number of exocytotic holes were found on the surface of podocytes by low vacuum electron microscopy.

Conclusions: In conclusion, podocyte vesicle transport could play an important role in the selective albuminuria in the minimal change nephrotic syndrome.

SUN-004
THE REGULATION OF THE GUT-KIDNEY AXIS IN VIVO BY TOTAL FLAVONE OF ABELMOSCHUS MANIHOt, A NATURAL EXTRACT, CONTRIBUTES TO THE AMELIORATION OF ADENINE-INDUCED RENAL FAILURE

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Introduction: Targeting gut microbiota dysbiosis and uremic toxins accumulation is important for the amelioration of renal dysfunction in chronic renal failure (CRF). Total flavone of abelmoschus manihot (TFA), a natural extract, has been applied extensively for treatment of the CRF patients in China. However, its therapeutic mechanisms remained elusive. Therefore, in this study, using an adenine-induced renal failure (RF) rat model, we examined the effects of TFA on the gut-kidney axis capture and high throughput illumina sequencing to obtain about 8 million sequences per sample. The Qiagen Biomedical Genomics Workbench software was used to identify InDels > 3 bp and > 20 sequences present exclusively in the patient population. One of the InDels identified was replicated in cultured podocytes using CRISPR Cas9 technology to study changes in ZHX2 expression.

Results: We identified 5 InDels (size range 6 to 67) shared by than one patient and 40 others (size range 4 to 133) present in a single patient. These InDels were absent in controls and the 1000 genomes project. Patients with MCD and FSGS tip lesion had a high percentage of deletions (approximately 80%), whereas those with other forms of FSGS had mostly insertions (approximately 66%). Significance of these indels was verified by inserting one of these indels upstream of ZHX2 in single cell derived immortalized human podocytes by CRISPR-Cas9 approach. Podocytes carrying this InDel developed reduced ZHX2 expression.

Conclusions: Insertions and deletions upstream of the ZHX2 gene are commonly present in patients with MCD and FSGS patients and alter ZHX2 mRNA expression.

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exosomes release.

**Methods:** Rats were randomly divided into 4 groups, the Sham-operated group, the Vehicle-treated group and the LUB-treated group. TFA, LUB and saline were daily administered for 4 weeks to induce glomerular injury in RF by adenine gavage with unilateral ureteral obstruction (UOO). Renal injuries and dysfunctional indicators, tubulointerstitial fibrosis (TIF), fecal microbiota, gut-derived uremic toxins, colon histological characteristics and tight junction proteins expressions, as well as the key protein expression levels of TLR4/NF-κB/NLRP3 inflammasome pathways in the colon and the kidneys were examined, respectively.

**Results:** In the RF model rats, in addition to renal lesions and uremic toxins accumulation, the abundance of Lactobacillus in the gut was decreased, while that of C. perfringens in the gut was increased; There appeared the ulcers in the colon, accompanied with the low-expression of ZO-1 and claudin-1; Besides, TLR4/NF-κB/NLRP3 inflammasome pathways in the colon and the kidneys were activated, respectively. After the treatment of TFA or LUB, renal dysfunction and TIF in the RF model rats were significantly improved. Furthermore, the disordered Lactobacillus, Enterococcus, E. coli and C. perfringens in the gut, the damaged intestinal environment and the accumulative indoxyl sulfate and p-cresyl sulfate in serum were all ameliorated. More notably, TFA synchronously inhibited TLR4/NF-κB/NLRP3 inflammasome pathway activity in the colon and the kidneys, whereas, LUB only suppressed TLR4/NF-κB/NLRP3 inflammasome pathway activity in the colon.

**Conclusions:** TFA, as a natural regulator in vivo, regulates the gut-kidney axis and ameliorates renal dysfunction in the RF model rats by modulating gut microbiota, reducing uremic toxins and inhibiting TLR4/NF-κB/NLRP3 inflammasome pathways activity in the colon and the kidneys, which is different from LUB. These findings may provide the first evidence for the gut-kidney axis, as the unusual target of TFA treatment in CRF.

**SUN-005**

**INCREASED URINARY EXOSOMAL miR-193A INDICATES PRIMARY FSGS POSSIBILITY AND POOR PROGNOSIS IN NEPHROTIC CHILDREN**

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**Introduction:** Focal segmental glomerulosclerosis (FSGS) is one of the most common primary glomerular diseases that cause end-stage renal disease in children. Exosomes are known to mediate intercellular communication by transporting cell-derived proteins and nucleic acids, including various miRNAs. Here we examined the levels of urinary exosomal miR-193a (Uexo-miR-193a) from patients with primary FSGS, and evaluated the values for diagnosis and prognosis.

**Methods:** Urine samples from eight primary FSGS patients were compared with those from minimal change nephropathy (MCN) and IgA nephropathy (IgAN) patients. Exosomes were isolated and confirmed by electron microscopy and western blotting. The level of miR-193a was quantified by qRT-PCR. ROC curves were applied to evaluate the diagnostic and prognostic values of Uexo-miR-193a in primary FSGS. The semiquantitative glomerulosclerosis index (GSI) was used to evaluate the degree of glomerulosclerosis according to the method of Raij et al. The expression of CD63 was detected with tubulointerstitial fibrosis (TIF), fecal microbiota, gut-derived uremic toxins, colon histological characteristics and tight junction proteins expressions, as well as the key protein expression levels of TLR4/NF-κB/NLRP3 inflammasome pathways in the colon and the kidneys were examined, respectively.

**Results:** The level of Uexo-miR-193a in primary FSGS patients was significantly higher than in MCN and IgAN patients. The area under ROC curve for Uexo-miR-193a was 0.85 and 0.821 respectively, which appeared to be a good marker to distinguish primary FSGS from other proteinuric glomerular diseases (MCN and IgAN). Moreover, Uexo-miR-193a levels positively correlated with GSI in primary FSGS patients. From 10 FSGS renal tissue samples, we further found that increased CD63 (exosome surface antigen) expression was detected in podocytes in non-sclerotic glomeruli. In vitro, podocyte-derived exosomes can deliver miR-193a to recipient cells, and a calcium-dependent mechanism is involved in the release of exosome in podocyte.

**Conclusions:** Urinary exosomal miR-193a might be a promising non-invasive diagnostic and prognostic marker for primary FSGS. Podocyte-derived exosomes can transport miRNAs to the recipient cells. A calcium-dependent mechanism is involved in the regulation of exosome release in podocyte.