Introduction: IgA nephropathy is one of leading causes of chronic kidney disease. Interstitial lesion in IgA nephropathy is correlated with unfavorable prognosis. Sensitive biomarkers are important for early detection and intervention targets of the disease. This study aims to identify Complement Receptor 1 (CR1) as a potential therapeutic target in IgA nephropathy patients with interstitial lesion.
Methods: Renal tissue proteomics data is accessed from a local IgA nephropathy cohort with 59 IgA nephropathy patients and 19 healthy controls. CD21/35$^+$B cells are separated with fluorescence activated cell sorting from mice spleen. Adaptive transfer is operated with a single injection from the renal vein immediately after urethral obstruction. Renal pathology is evaluated on pictures captured by a visual microscope.
Results: CR1 is identified as the most significantly downregulated complement component in IgA nephropathy patients.

Clinical information characterization of IgA nephropathy patients is assessed with Pearson R correlation test to confirm their linear independence. Of the 28 complement components recognized, 24 protein expression is increased in IgA nephropathy patients and 4 is decreased compared to healthy control. CR1 is identified as the most significantly decreased complement component in IgA nephropathy patients.

CR1 protein expression is inversely correlated with IgA nephropathy interstitial lesion but not with renal function progress.

Further correlation analysis of clinical information reveals that CR1 protein expression is inversely correlated with IgA nephropathy interstitial lesion, as represented as Oxford Classification T score. However, CR1 is not significantly correlated with serum creatine level or renal function loss progress (calculated as average eGFR decline per month).

CD21/35$^+$ cells are increased in the experimental renal interstitial injury mice.

To test the hypothesis CR1 may be associated with interstitial lesion, we study the CD21/35 (CD21/35 is the mouse homolog of CR1 molecule) expression in unilateral urethral obstruction mice. We find that CD45$^+$bone marrow derived cells significantly infiltrated the obstructed kidney at day 12, of which the CD5$^+$ CD21/35$^+$cells significantly increased compared to control.

Adaptive transfer of CD21/35$^+$B cells protects the cortex structure in experimental renal interstitial injury.

To test whether the CD21/35 molecule on immune cells are protective against interstitial lesion, we sorted CD21/35$^+$B cells and CD21/35$^-$B cells and test their respective protective potential through adaptive transfer into UUO mice. We find that the renal cortex width is significantly increased in CD21/35$^+$group than that in CD21/35$^-$group at day 12 after UUO.
Conclusions: CR1 is inversely correlated with renal interstitial lesion in IgA nephropathy patients and is potentially protective in experimental renal interstitial injury.

No conflict of interest

POS-408

CARNOSINE ALLEVIATES PODOCYTE INJURY IN DIABETIC NEPHROPATHY BY TARGETING CASPASE-1-MEDIATED PYROPTOSIS

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Introduction: Carnosine is a dipeptide consisting of β-alanine and L-histidine. Studies have shown that carnosine has strong anti-inflammatory ability in AKI. In diabetic animals, carnosine improves the histology and function of mesangial cell. Combined, these functions indicate that carnosine has the potential for development as a drug to treat DN. However, the specific mechanism of carnosine relative to podocyte injury in DN remains unclear and requires further exploration. The current study aimed to evaluate the protective effects of carnosine on glomerular podocytes in DN, both *in vivo* and *in vitro* .
Methods: In vivo experiment, we constructed the diabetic model by intraperitoneal injection of streptozotocin (STZ) in mice, and carnosine was given 1g/kg treatment. After 12 weeks of rearing, the 24-hour urine protein was tested to confirm the success of the diabetic nephropathy model, and the general indicators and pathological changes of the mice were tested. The changes of renal podocyte markers nephrin, podocin, WT-1, inflammation and pyroptosis were detected by immunohistochemistry, Western blot, Real-time PCR and other methods.

In vitro experiments, we used high glucose (30mM) to induce renal podocyte (MPC5) injury, and screened the cytoprotective effect of carnosine by MTT. Western blot, immunofluorescence, Real-time PCR and other methods were used to detect renal podocyte markers nephrin and podocin; inflammation-related indicators NLRP3, ASC, IL-1β, IL-18; pyroptosis key protein Caspase-1, GSDMD expression changes. The combination of carnosine and Caspase-1 was verified by molecular docking and Cellular Thermal Shift Assay (CESTA). Silencing Caspase-1 with siRNA to detect whether carnosine exerts its protective effect by targeting Caspase-1.
Results: In vivo experiments showed that carnosine can reduce the general indicators of diabetic nephropathy and kidney pathological changes, reverse the damage of renal podocytes, and reduce the renal inflammation and pyroptosis. In vitro experiments used MTT to screen the optimal concentration of carnosine to be 40μM. Carnosine reversed the expression of renal podocyte damage and inflammation-related indicators NLRP3, ASC, IL-1β, and IL-18. Carnosine can reduce the level of cell pyroptosis, which is manifested as carnosine can significantly reduce the GSDMD and Caspase-1 of podocytes under high glucose stimulation.

Molecular docking and CESTA confirmed that Caspase-1 is a possible target of carnosine. In the state of silencing Caspase-1, carnosine cannot reverse the damage of kidney podocytes induced by high glucose.
Conclusions: Carnosine reduces the development of diabetic nephropathy by targeting inflammation and pyroptosis mediated by Caspase-1.

No conflict of interest

POS-409

IDENTIFICATION OF IMPORTANT PATHOLOGICAL MRNA AND MICRORNA TRANSCRIPTS INVOLVED IN WILMS TUMOR AND RHABDOID TUMOR OF THE KIDNEY USING ASSOCIATION RULE MINING

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Introduction: Wilms tumor (WT) and rhabdoid tumor of the kidney (RT) are respectively the most and less common types of pediatric kidney tumors. Due to the presence of overlapping histologic patterns and similar cell types across these tumors, their differential diagnosis solely based on histologic study can be challenging. To this end, this study aimed to apply machine learning and deep learning algorithms to identify the most important mRNAs and microRNAs panels that can be involved in the pathogenesis of the WT and RT.
Methods: The RNA transcripts including 1881 microRNA (miRNAs) and 60,482 mRNAs obtained from 126 and 199 patients, respectively, were downloaded from The Cancer Genome Atlas (TCGA) dataset. To identify candidate features (mRNAs and miRNAs), graph and filter algorithms were used in feature selection. Then, a deep model was used to classify the tumors. Finally, an association rule mining algorithm was used for detecting the most significant mRNAs/ miRNAs involved in the pathogenesis of the WT and RT.
Results: In the classification step, candidate miRNAs could classify the WT and RT classes in train/test data with high accuracy (97% / 93%). Candidate mRNAs could also classify the WT and RT classes in train/test data with high accuracy (94% / 97%) and AUC (≥0.95). The Association Rule Mining analysis could identify the Chromosome 19 open reading frame 24 (C19orf24) and let-7a-2 as well as the RP1-3E10.2 and miR-199b as first top transcripts in the WT and RT, respectively.
Conclusions: The employed framework can offer further insight into the pathogenesis, diagnosis, prognosis, and therapeutic targets in pediatric kidney tumors.

No conflict of interest