ingegneria sismica
International Journal of Earthquake Engineering
Anno XLIII - Num. 3 - 2026

Combining bioinformatics and algorithmic modeling to study the intestinal-kidney axis regulatory mechanism in chronic kidney disease

Xueying Li[1,*]

[1] China Medical University, Shenyang, Liaoning, 210100, China

SUMMARY: *Immunoglobulin A nephropathy (IgA) is one of the most common primary glomerular diseases and a common predisposing cause of chronic kidney disease. In this paper, using IgA nephropathy as an entry point, we use the New Entity Embedding Representation Algorithm based on Graph Attention Networks (NEEGAT) to solve the problem of the continuous emergence of new entities in the bioinformatics knowledge graph. The algorithm obtains the semantic information in the graph after TransE pre-training, introduces the knowledge graph by means of logical attention, and integrates the inter-section connectivity relations using graph attention to obtain the embedding representation of new entities. The weighted gene co-expression network analysis (WGCNA) method was also selected to identify the modular genes highly associated with IgA nephropathy. The identification and determination of IgA nephropathy was proposed by integrating the pathogenesis of IgA nephropathy under the intestinal-renal axis. Using the designed method to assist the application of the receptor of adenosine A2A in the treatment of IgA nephropathy, the obtained receptor of adenosine A2A was able to promote the increase of the expression level of the receptor α-SMA (up to 53.89% at day 14) and the decrease of the expression level of E-cadherin (up to 40.00% at day 14).*

KEYWORDS: *new entity embedded representation; IgA nephropathy; WGCNA method; bioinformatics; intestinal-kidney axis*

1 Introduction

Chronic kidney disease (CKD) is defined as progressive and irreversible loss of renal function, as evidenced by the presence of markers of renal damage lasting more than 3 months, with or without glomerular filtration rate [1]. CKD is a slowly developing clinical syndrome with gradual deterioration of renal function, which is characterized by a complex pathogenesis, prolonged disease course, and a severe and often persistent progression to end-stage renal failure, which is a serious hazard to CKD is a serious threat to human life and health [2-4]. Delaying or interrupting the progression of CKD has become an important challenge for the clinical medical community and health departments of various countries.

According to the theory of “intestinal and renal axis” in Chinese medicine, there is a close relationship between the intestines and the kidneys, which influences and regulates each other, and the adjustment of intestinal peristalsis can help to restore renal function [5]. The “gut-kidney axis” theory reflects the two-way communication between gut microorganisms and CKD, and the two influence each other in an interactive way. On the one hand, CKD significantly alters the composition and function of gut microbes, leading to dysregulation of

*lxyscientificpaper@163.com
https://doi.org/10.65102/is20261082 Published: 10 June, 2026

gut ecology [6]. On the other hand, gut microorganisms accelerate the migration of renal disease and clinical malignancy through the accumulation of a series of metabolites that cause the body to produce inflammatory reactions, endocrine disorders, and damage to the intestinal barrier function [7, 8]. Based on this theory and the close connection between intestinal microecology and CKD, nutritional and pharmacological interventions targeting intestinal flora have obvious improvement effects on metabolic syndromes such as CKD [9-11]. Up to now, modern medicine still lacks an ideal treatment for this disease, while Chinese medicine has accumulated rich clinical practice experience in the treatment of CKD, which can effectively improve renal function and delay renal failure, and has unique advantages [12-15]. Exploring the role played by the intestinal-kidney axis theory in the development of chronic kidney disease can provide an important theoretical basis for exploring new strategies for the clinical treatment of chronic kidney disease based on intestinal microecology.

In this paper, we first describe the input layer, transposition layer and logical aggregation layer in the new entity embedding representation algorithm based on graph attention network in order. Then, we use the WGCNA method to identify modular genes that are highly related to IgA nephropathy, and explain the construction process of gene-gene similarity network and the steps of identifying co-expressed gene modules. Meanwhile, we analyze the understanding of the pathogenesis of IgA nephropathy in Chinese medicine, and comprehensively propose a method for the identification and determination of IgA nephropathy. Finally, with the support of the proposed methodology, the effects of adenosine A2A receptor and umbilical cord mesenchymal stem cell exocytosis in the treatment of IgA nephropathy were investigated based on the experiments with small (large) mice.

2 Methods of recognizing and determining IgA nephropathy

2.1 New Entity Embedding Representation Algorithm Based on Graph Attention Networks

Knowledge representation is a very important research element of knowledge graph and the basis for many downstream tasks such as knowledge reasoning and intelligent Q&A. Taking knowledge reasoning as an example, assuming that the embedded knowledge representations of all entities and relations in the knowledge graph have been acquired, for a new triple (s,o,r), if the knowledge representations of both the head entity s and the tail entity o are known, the type of the relation of r can be inferred. The knowledge representation of the knowledge graph can be obtained using Deep Walk, node2vec and other methods, but these methods can only deal with static graphs, i.e., graphs in which both the entities and relationships are no longer changing. However, in practical application scenarios, with the change of time, the knowledge graph will often have new entities. Faced with this situation, traditional static coding methods can only incorporate new data and retrain the model with all the data. This will not only increase the settlement of the model in practical applications, but also make the prediction results uncertain and bring a large number of problems to the downstream tasks. The domain knowledge graph of bioinformatics tools constructed in this paper is necessary for the knowledge representation of out-of-knowledge-base (OOKB) entities because the iterative updating of bioinformatics tools is fast, and new entities will appear frequently in the process of using them. In this paper, based on the inductive knowledge graph embedding method based on logical attention neighborhood aggregation, a graph attention network is introduced, i.e., after generating new entity embedding vectors by the logical attention module, a so-called “New Entity Embedding Representation Algorithm

Based on Graph Attention Networks (NEEGAT)" is proposed by using the graph attention network as an aggregator, which further aggregates the neighborhood features ".

2.1.1 Input layer

Assume that the knowledge graph G consists of a series of triples: $G=\{(h,r,t)\mid h\in E,r\in R,t\in E\}$, and E and R denote the set of entities and relations, with the number of entities being n and the number of relations being m. In this paper, TransE is used to initialize the knowledge graph and trained to obtain the entity embedding vector matrix $M_e\in\mathbb{R}^{n\times d}$ and the relation vector matrix $M_r\in\mathbb{R}^{m\times d}$.

If (h,q,t) is a newly added triad in the knowledge graph G, its head entity h and tail entity t are assumed to be new entities for the sake of exposition. In the input layer, the knowledge graph is first searched to obtain the sets of neighboring nodes $N_k(h)$ and $N_k(t)$ for the head entity h and the tail entity t, whereupon the corresponding vectors of the neighboring entities of h in M_e are used as their input vectors in the input layer, respectively. That is, for any node $e_j\in N_k(h)$, its corresponding input vector is equation (1):

$$x_j=QM_e \tag{1}$$

where $Q\in\{0,1\}^n$ is an n-dimensional one-hot vector with only one component of 1, denoting the entity number corresponding to the entity in M_e. The same operation is performed for the tail entity t.

All relations are inverted in the input layer to compensate for the sparsity of the data, i.e., if the triple (h,r,t) exists, the data is expanded by adding the triple (t,q^{-1},h).

2.1.2 Transposition layer

The purpose of the transposition layer is to perform a feature transformation of the embedding x_j of the neighbor node of the input layer against the relation r based on the relation r between the new entity and its neighbor node. In order to react to the influence of relation r on this neighbor node, a transformation vector W_r related to relation r is used to transform its embedding x_j, which is computed as in Equation (2):

$$y_j^t=x_j-W_r^Tx_jW_r \tag{2}$$

where y_j^t represents the transformed vector of neighboring node j and W_r represents the relation-specific transformation vector and is restricted to be a unit vector.

2.1.3 Logical aggregation layer

In the logical aggregation layer, the overall information of the knowledge graph is used as the logical attention to weight the aggregation of the neighboring entities of the new entity. A confidence calculation is defined in LAN, which is calculated as in Eq. (3), for a node e, which has the neighboring relationships r_1,r_2, there may be an inclusion relationship of information, and their potential association rules are remembered as $r_1\Rightarrow r_2$:

$$\mathcal{P}(r_1 \Rightarrow r_2) = \frac{\sum_{e \in E} \mathbb{I}(r_1 \in N_R(e) \wedge r_2 \in N_R(e))}{\sum_{e \in E} \mathbb{I}(r_1 \in N_R(e))} \tag{3}$$

where $N_R(e)$ represents the set of relations of node e, and $\mathbb{I}(x)$ takes either 1 or 0 only, 1 when e is adjacent to both relations, 0 otherwise.

Confidence is calculated from the whole knowledge graph, $\mathcal{P}(r_1 \Rightarrow r_2)$ value is large indicates that there are more neighboring nodes overlap between r_1 and r_2, in the training phase, the confidence can be calculated first.

In order to obtain the initial embedding vector h^l of the new entity h, for each j in the set of neighboring nodes $N_k(h)$, the weight $\alpha_{j|h,q}$ is calculated, and $\alpha_{j|h,q}$ stands for the influence of the neighboring node j on the node h when the new node is h and the relationship of the new triad is q. Inspired by the LAN model, the customized logic rules in the LAN model are used to calculate the weights $\alpha_{j|i,q}$ of neighboring nodes as in Equation (4):

$$\alpha_{j|h,q} = \frac{\mathcal{P}(r \Rightarrow q)}{max(\{\mathcal{P}(r' \Rightarrow r) \,|\, r' \in N_R(h) \wedge r' \neq r\})} \tag{4}$$

The embedding vector h^l of the final new node h is equation (5):

$$h^l = \sum_{(r,e_j) \in N_k(h)} \alpha_{j|h,q} y_j^t \tag{5}$$

Similarly the embedding vector t^l of the new node t can be obtained as equation (6):

$$t^l = \sum_{(r,e_j) \in N_k(t)} \alpha_{j|t,q} y_j^t \tag{6}$$

2.2 WGCNA identifies disease-associated primary module genes

In this study, weighted gene co-expression network analysis (WGCNA) method was used to identify gene modules highly associated with IgA nephropathy.WGCNA identifies co-expressed genes by utilizing the idea of weighting to form different co-expressed gene modules and combining the associations of the modules with extrinsic traits in order to discover module genes highly correlated with extrinsic traits. It generally consists of four steps: constructing gene-gene similarity networks, identifying co-expressed gene modules by clustering the co-expressed genes, determining the association of the gene modules with external traits, and identifying the core genes in the modules.

The dataset GSE93798 contains tens of thousands of genes, and the data were preprocessed to increase the computational efficiency. Firstly, the “good Samples Genes” function was used to detect whether there were genes and samples with too many missing values in the data and eliminate them. The genes with large standard deviation of expression (the top 25%) were then selected for subsequent analysis, and the outliers were detected by sample clustering and eliminated.

2.2.1 Constructing gene-gene similarity networks

WGCNA constructs a similar expression matrix by calculating the Pearson correlation coefficient between two genes and setting a soft threshold to determine whether there is a similar expression pattern between them. Since in the real biological regulatory network, only a few some genes play very important some regulatory roles, i.e., the gene regulatory network is more consistent with the scale-free network. A scale-free network is a network in which the connectivity between nodes has a severe inhomogeneity, with a few key nodes having a very large number of connections (edges), and the majority of nodes being connected to only a few other nodes. Scale-free networks are robust in the sense that the network faces collapse only when these few critical nodes are removed and remains stable when non-critical nodes are removed. Therefore, WGCNA uses the idea of "weighting", i.e., a power operation on the correlation coefficients, where the value of the power is defined as a soft threshold. This power operation enhances the strong correlation between genes at the expense of the weak correlation of genes, making the correlation values more consistent with the scale-free network characteristics and more biologically meaningful. If the traditional hard threshold is used to determine whether two genes have similar expression, i.e., the correlation coefficient of two genes is defined as correlation if it is greater than this threshold, and as irrelevant if it is less than this threshold, it is impossible to assess the correlation of two genes that are slightly less than or slightly greater than this threshold, resulting in the loss of important information. The use of soft thresholds instead of hard thresholds compensates for the fault of "one size fits all".

The built-in "pick Soft Threshold" function in the WGCNA package is used to establish the optimal soft threshold. Then the following formula is used to calculate the neighboring coefficients, and the similar expression matrix is converted into a weighted neighboring matrix, i.e., the matrix composed of the weighted correlation values between genes and genes, and a network conforming to the scale-free distribution is constructed with equation (7):

$$S_{ij} = \left| cor(X_i, X_j) \right| \; A_{ij} = \left| S_{ij} \right|^{\beta} \tag{7}$$

Note: X_i: i genes, X_j: j genes, S_{ij}: Pearson's correlation coefficient between i genes and j genes, A_{ij}: neighbor-joining coefficient between i genes and j genes, and β denotes the soft threshold.

2.2.2 Identifying co-expressed gene modules

Since the correlation coefficient only takes into account the linear relationship between two genes, but when evaluating the correlation of two genes, we cannot only look at the expression correlation of two genes, but also take into account their interactions with other genes. Therefore, the "blockwise Modules" function was further used to convert the weighted neighbor matrices of the genes into topological overlap matrices (TOMs) to represent the similarity of the genes at the network topology level. Topological overlap is a method to quantitatively describe the similarity between nodes by comparing the weighted correlation between two nodes and other nodes in the network. Converting the adjacency matrix to a topological overlap matrix reduces noise and false correlations. Subsequently, hierarchical clustering was performed using the "plot Dendro and Colors" function to transform thousands of genes into several co-expressed gene modules and merge the more closely expressed modules into a new module.

3 Mechanisms of intestinal-kidney axis regulation in IgA nephropathy from the perspective of Chinese medicine

According to the clinical manifestations of IgA nephropathy, TCM classifies it into the categories of "edema", "kidney strain", "low back pain" and "kidney wind". The causes of IgA nephropathy are mainly spleen and kidney disorders, invasion of external evils and deficiency of vital energy and internalization of turbid toxins. Su Wen - The Treatise on the Method of Stabbing says, “When righteousness exists within, evil cannot be interfered with.” The "Ling Shu: The Beginning of All Diseases" states: "Wind and rain, cold and heat cannot be vain, and evil cannot hurt people alone. Those who are not sick in the face of a storm and rain are covered without emptiness, so evil cannot hurt people alone, and this must be due to the wind of vanity and evil, and its body, the two voids are compatible, and it is the shape of the object.” It can be seen that the main reason for the development of IgA nephropathy is the dysfunction of the lungs, spleen and kidneys, coupled with exogenous six evils and other poisonous evils to take advantage of the situation. The internal organs cooperate with each other physiologically and influence each other pathologically. Lung is the source of water, the main hair purging, the body's water transmission, operation and excretion has an important role. Kidney is a water organ, the main fluid metabolism, the lungs and kidneys for each other, and the spleen's main function of transporting water and humidity, to maintain the normal operation and metabolism of water. If the spleen fails to elevate and clear, and the kidney fails to seal and hide, the essence will be leaked and the essence material will leak out from the urine, resulting in frequent urination, continuous increase of urinary proteins, and hypoproteinemia. If the qi does not take in blood, the blood does not follow the meridian, overflows outside the veins, seeps into the bladder, and develops into hematuria; if the lungs are not pronounced and purified, and the spleen is not transported, the metabolism of the body's fluids is impaired, resulting in the internal storage of water and dampness, and the overflow of the skin develops into edema. Some scholars believe that the function of the spleen and stomach in Chinese medicine is consistent with the physiological function of the intestines in Western medicine, and the disease of IgA nephropathy is located in the spleen and kidney. Based on the holistic view of Chinese medicine and the method of diagnosis and treatment, the treatment can be based on spleen and kidney.

Another factor of IgA nephropathy is the deficiency of positive qi and the internalization of turbid poison. Su Wen - General Commentary on the theory of emptiness and realism says: “If the essence is taken away, then there is emptiness.” "Zhengzhi Huibu" said: "The void is the emptiness of the flesh; The damage to the viscera is also.” Prof. Huang Chunlin believes that although the pathogenesis of chronic kidney disease is complex, it is mainly due to the internalization of turbid poison, which ultimately leads to kidney qi failure. On the basis of the theory of “Prana Gate is also the ambassador of the five organs”, Prof. Zhu Caifeng believes that if the Prana Gate is not open, the turbid qi congestion will lead to kidney qi deficiency, which will aggravate the turbid toxicity in IgA Nephropathy patients, and make it difficult to get rid of the real evils such as wind-dampness and blood stasis. The current concept of “intestinal-kidney axis” in modern medicine also suggests a close relationship between prana and IgA nephropathy. Patients with IgA nephropathy are prone to infections, hypercoagulable state and edema, which are caused by immunocompromise and hypoproteinemia, etc. As the condition lasts for a long time, the permeability of intestinal mucosa is further damaged by intestinal toxins and pathogenic bacteria, which invade into the bloodstream and cause renal injury, which further deteriorates the renal function. The deficiency of positive energy and the entry of disease evils into the interior of the body produce “poison” as the main pathological product at various stages, leading to the occurrence

of IgA nephropathy, and its prolonged treatment leads to the exhaustion of the true essence of the kidneys, which results in the development of end-stage nephropathy.

4 Regulatory mechanisms based on IgA nephropathy recognition methods

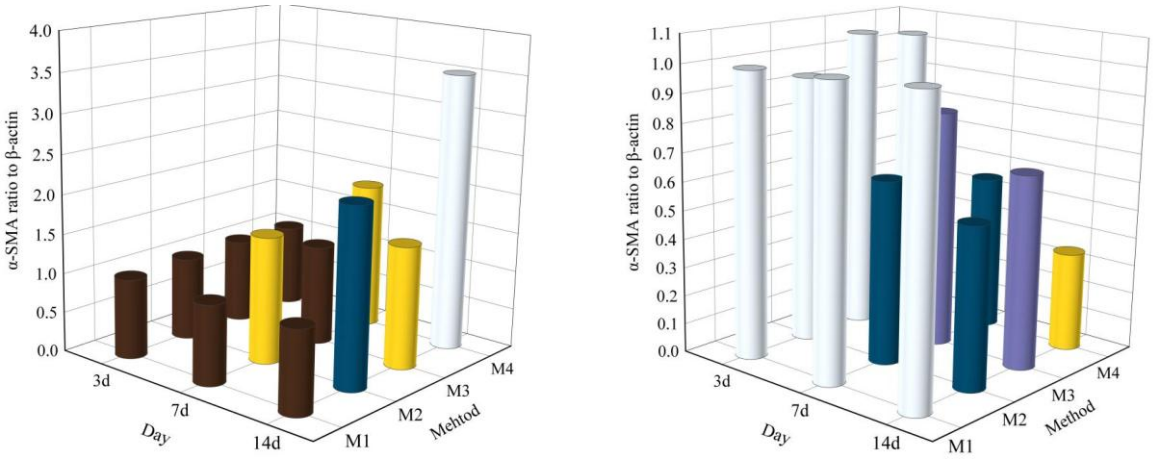
4.1 Therapeutic effects of receptors for adenosine A2A

Epithelial-to-mesenchymal transition (EMT) is an important mechanism for tumor cell progression and metastasis, and in this paper, inhibition/reversal of the EMT state is used as the mainstay of treatment for chronic kidney disease. In this regard, the receptor for adenosine A2A was introduced to assist the treatment, and the receptor for adenosine A2A ($A_{2A}R$), as a new inflammatory regulator regulating the inflammatory process and tissue repair, can effectively inhibit inflammation in the current practical application. Glomerulonephritis and kidney injury can be attenuated by activating $A_{2A}R$. In this section, based on the experimental setting of the mouse UUO model, the changes in the markers of renal tubular epithelial cells (E-cadherin) and the surface markers of myofibroblasts (α-SMA) were analyzed with the assistance of the above mentioned methods of identifying and determining IgA nephropathy.

4.1.1 $A_{2A}R$ activation inhibits the EMT process

Activation of $A_{2A}R$ activity modulated the expression of α-SMA and E-cadherin in the UUO model shown in Figure 1, where (M1) Sham, (M2) UUO+Veh, (M3) UUO+CGS, and (M4) UUO+KO.

Westernblot analysis showed that at 3 days after UUO, the expression of α-SMA and E-cadherin did not differ between the individual UUO groups and the sham operation group. As can be seen in Figure 1: $P>0.05$,n=5/group, suggesting that the EMT process did not occur. Notably, the expression level of α-SMA in the UUO wild control group (M2) was increased by 59.12% (day 7), and 126.1% (day 14) compared to the sham-operated group ($P<0.05$,n=5/group), however, the expression level of E-cadherin was decreased by 35.3% (day 7) and 42.87% (day 14 days) ($P<0.05$,n=5/group). Importantly, α-SMA levels decreased by 21.67% (day 7), 31.28% (day 14) in the $A_{2A}R$ agonist-treated group compared to the UUO wild control (M2) group ($P<0.05$,n=5/group). On the contrary, CGS21680 increased the expression level of E-cadherin by 28.03% (day 7) and 20.57% (day 14) compared with M2 group ($P<0.05$, day7 and day14, n=5/group). On the other hand, $A_{2A}R$ inactivation (M4) led to completely opposite effects in the expression levels of α-SMA and E-cadherin compared to $A_{2A}R$ activation (M3). Compared with the M2 group, the expression levels of α-SMA increased by 18.04% (day 7) and 53.89% (day 14), whereas the expression levels of E-cadherin decreased by 15.64% (day 7) and 40.0% (day 14), respectively, ($P<0.05$, day7 and day14, n=5/group). In conclusion, $A_{2A}R$ activation-induced decrease in α-SMA and rise in E-cadherin confirmed the inhibition of EMT process in renal tubular epithelial cells by $A_{2A}R$.

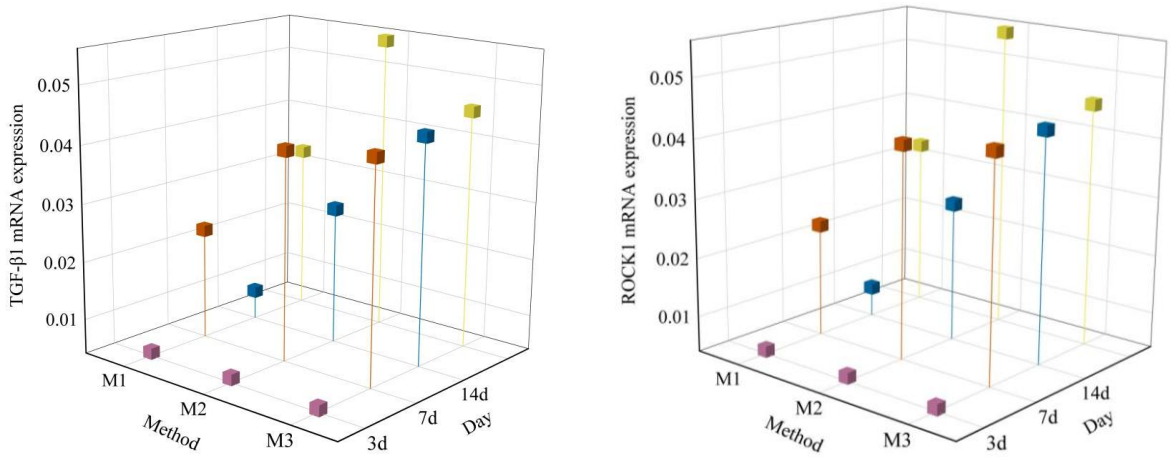


(a) α-SMA ratio to β-actin (b) E-cadherin ratio to β-actin

Figure 1: The expression of α-SMA and E-cadherin in the model

4.1.2 Activation of $A_{2A}R$ reduces the expression of pro-fibrotic factors

To further assess the regulatory mechanism of $A_{2A}R$ on renal interstitial fibrosis, the expression of two key pro-fibrotic factors, TGF-β1 and ROCK1, was examined using RT-qPCR. The results, as shown in Figure 2, showed that the TGF-β1 mRNA expression level was significantly increased in the M2 wild control group compared with that in the sham operation from 3 to 14 days after UUO (408%,789%, and 833%, respectively, at 3, 7, and 14 days after UUO) ($P<0.05$, n=10/group). However, the increase in TGF-β1 mRNA expression level was significantly suppressed in the $A_{2A}R$ agonist-treated group (M3), decreasing by 61.2% ($P < 0.05$) and 30.8% ($P < 0.05$) at 3 and 7 days after UUO surgery, respectively, compared with the UUO wild control group (M2) (n=10/group). In contrast, inactivation of the $A_{2A}R$ gene resulted in a significant increase in TGF-β1 mRNA by 38.7% (3 days after UUO) and 37.5% (7 days after UUO) ($P < 0.05$, n = 10/group) compared with the UUO wild control (M2). Notably, the above $A_{2A}R$-mediated inhibitory effect on TGF-β1 expression disappeared at 14 days after UUO, which was not statistically different from the other UUO groups of mice, suggesting that activation of the $A_{2A}R$-induced inhibitory effect on TGF-β1 expression occurs only at the early and progressive stages, rather than at the late stage after UUO.



(a) TGF- β1 (b) ROCK1 mRNA

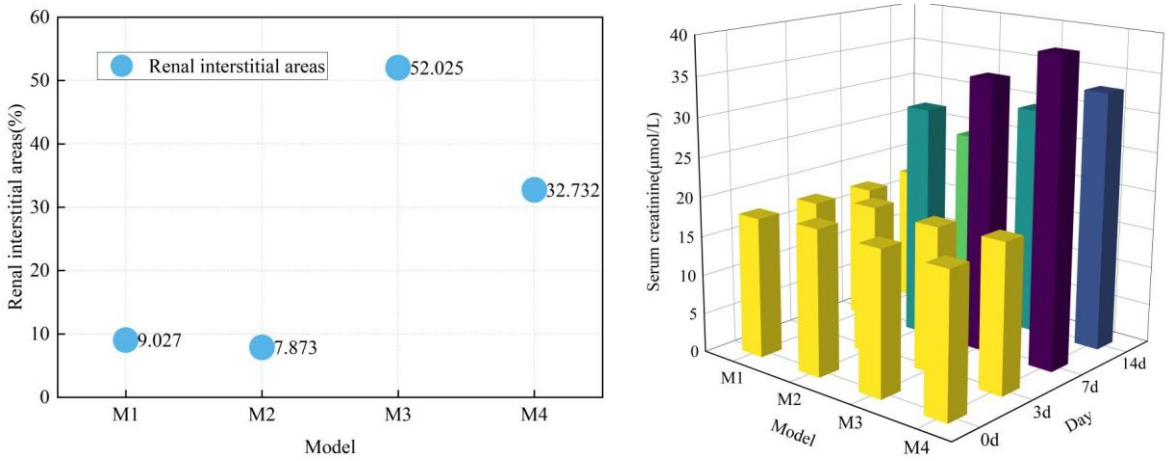
Figure 2: The expression of TGF- β1 and ROCK1 mRNA in the model

4.2 Analysis of the therapeutic effect of umbilical cord MSC exosomes

After obtaining the IgA disease-related gene module by combining the analytical methods mentioned in the second chapter with the knowledge of Chinese medicine on the pathogenesis of IgA nephropathy, we used rat ureteral obstruction to establish a model of chronic kidney disease in this section, and injected human umbilical cord mesenchymal stem cells (hucMSC-Ex) into the model by renal artery injection route. Next, the effects of hucMSC-Ex on the morphology and function of rat kidneys and the changes in autophagy levels of kidney tissues in rats with chronic kidney disease during treatment were analyzed, respectively. Among them, (M5) UUO+minmic NC, (M6) UUO+miR-146a-5p minmic, (M7) UUO+miR-146a-5p inhitor, (M8) UUO+inhitor NC, (M1)-(M2) were the sham-operated group (control group), (M3)-(M4) were the sham-operated group + exosomes (control+Ex group), (M5)-(M6) for model group (UUO group), and (M7)-(M8) for model+exosomes group (UUO+Ex group).

4.2.1 Effect of hucMSC-Ex on the morphology and function of rat kidney

The results of HE and PAS staining showed that the glomerular tubular structure was intact and no obvious abnormality was seen in the Control and Control+Ex groups, and the epithelial structure of the renal tubules in the UUO group was disrupted, with the appearance of detachments in the lumen of the tubules, obvious tubular dilatation, and a large number of inflammatory cells infiltrated in the renal interstitium, which was obviously reduced by the addition of the hucMSC-Ex intervention.Masson staining The results showed that the renal structure was intact and no obvious collagen fiber deposition was seen in the interstitium in the Control and Control+Ex groups, the renal structure was obviously damaged and a large number of collagen fibers were deposited in the interstitium in the UUO group, and the collagen fiber deposition was obviously reduced in the UUO+Ex group. The results of renal function tests showed that there was no significant difference in Scr and BUN in the Control and Control+Ex groups, and on days 3, 7, and 14 after modeling, Scr and BUN were progressively elevated in rats in the UUO group, and decreased significantly after hucMSC-Ex intervention. The effect of hucMSC-Ex on renal pathology and function in unilateral ureteral obstruction is shown in Figure 3.

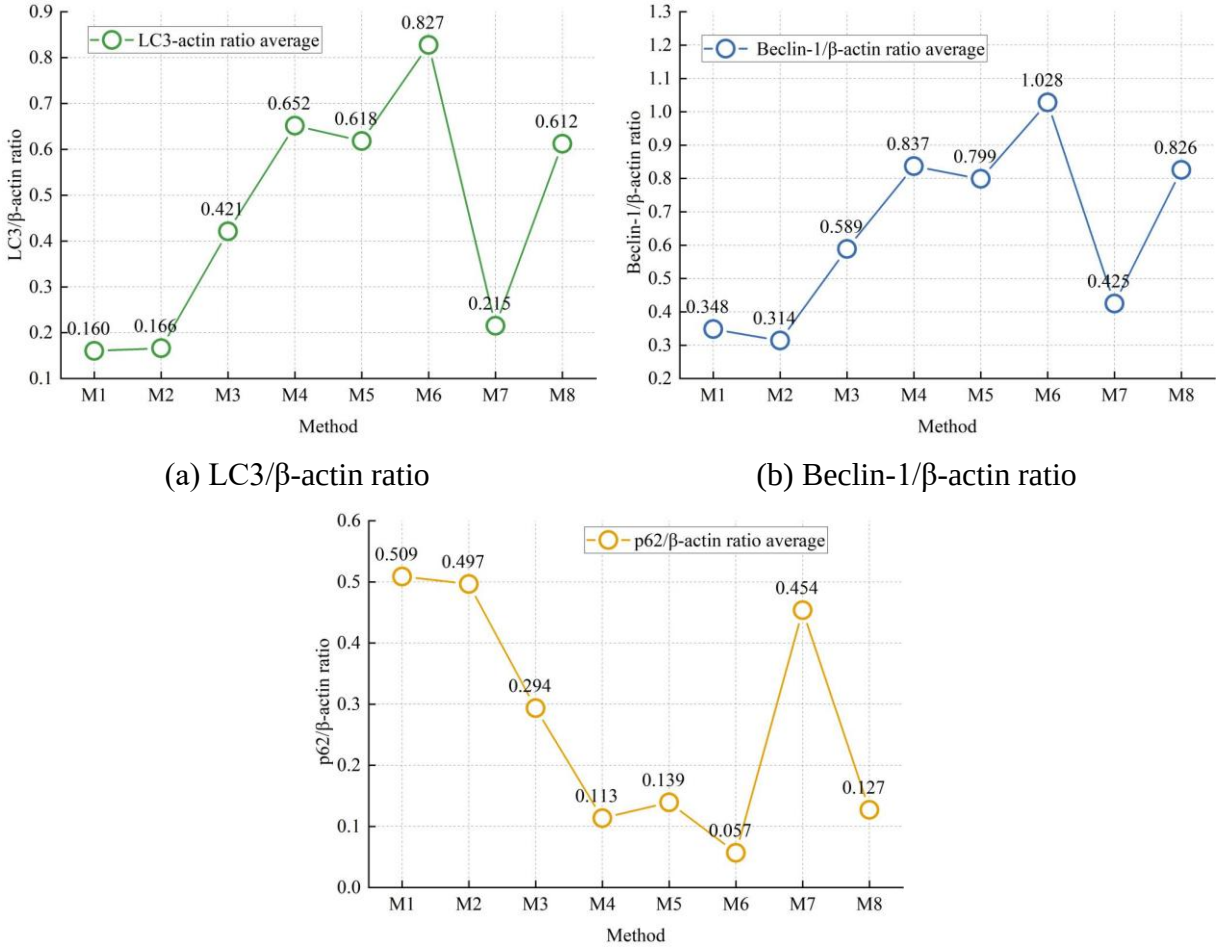


(a) Renal interstitial areas (b) Serum creatintine

Figure 3: The influence of hucMSC-Ex on renal pathology and function

4.2.2 Levels of autophagy in kidney tissue of rats with chronic kidney disease

Western blot results showed (Figure 4) that the expression of autophagy-related proteins LC3 and Beclin-1 increased and the level of autophagy substrate p62 decreased in the UUO group compared with the Control and Control+Ex groups, suggesting that autophagy was activated, and after hucMSC-Ex intervention, the expression of LC3 and Beclin-1 increased further and the level of p62 further decreased, suggesting that hucMSC-Ex promoted autophagy. Compared with the UUO+Ex group, the addition of miR-146a-5pmimic increased LC3 and Beclin-1 expression and decreased p62 levels, and after the addition of miR-146a-5pinhibitor, LC3 and Beclin-1 expression decreased and p62 levels increased, suggesting that miR-146a-5p can positively regulate autophagy development.



(a) LC3/β-actin ratio

(b) Beclin-1/β-actin ratio

(c) p62/β-actin ratio

Figure 4: The expression of LC3, Beclin-1 and p62 in renal tissues

5 Conclusion

In this paper, we design a new entity embedding representation method based on graph attention network for characterization generation of new entities in biological information. The WGCNA method is used to identify the core gene modules related to IgA nephropathy, and the IgA nephropathy identification and determination method is proposed by borrowing the knowledge of the pathogenesis of IgA nephropathy based on the intestinal-kidney axis in Chinese medicine.

With the support of the designed IgA nephropathy identification and determination method, experiments on the application of adenosine A2A receptor and umbilical cord mesenchymal stem cell exosomes in the treatment of IgA nephropathy were conducted successively. In the experiments, under the action of adenosine A2A, the expression levels of receptor α-SMA increased by 18.04% (day 7) and 53.89% (day 14), while the expression levels of E-cadherin decreased by 15.64% (day 7) and 40.0% (day 14), respectively. And umbilical cord MSC exosomes not only effectively prevented Scr and BUN expansion, but also positively regulated the development of renal autophagy.

References

[1] Romagnani, P., Remuzzi, G., Glassock, R., Levin, A., Jager, K. J., Tonelli, M., ... & Anders, H. J. (2017). Chronic kidney disease. Nature reviews Disease primers, 3(1), 1-24.

[2] Kovesdy, C. P. (2022). Epidemiology of chronic kidney disease: an update 2022. Kidney international supplements, 12(1), 7-11.

[3] Lv, J. C., & Zhang, L. X. (2019). Prevalence and disease burden of chronic kidney disease. Renal fibrosis: mechanisms and therapies, 3-15.

[4] Luyckx, V. A., Tuttle, K. R., Garcia-Garcia, G., Gharbi, M. B., Heerspink, H. J., Johnson, D. W., ... & White, S. L. (2017). Reducing major risk factors for chronic kidney disease. Kidney international supplements, 7(2), 71-87.

[5] Zhou, T., Zhang, Y., Li, Z., Lu, C., & Zhao, H. (2024). Research progress of traditional Chinese medicine on the treatment of diarrhea by regulating intestinal microbiota and its metabolites based on renal-intestinal axis. Frontiers in Cellular and Infection Microbiology, 14, 1483550.

[6] Kalantar-Zadeh, K., & Fouque, D. (2017). Nutritional management of chronic kidney disease. New England Journal of Medicine, 377(18), 1765-1776.

[7] Long, C., Zhang, C., & Xie, Y. (2024). Study on the mechanism of hirudin multi target delaying renal function decline in chronic kidney disease based on the “gut-kidney axis” theory. Naunyn-Schmiedeberg's Archives of Pharmacology, 397(10), 7951-7962.

[8] Li, J., Xu, Y., Sun, T., Zhang, X., Liang, H., Lin, W., ... & Yang, H. (2024). Exploration of the pathogenesis of nephrotic syndrome and traditional Chinese medicine intervention based on gut microbiota. Frontiers in Immunology, 15, 1430356.

[9] He, Y., Jia, D., Chen, W., Liu, J., Liu, C., & Shi, X. (2024). Discussion on the treatment of diabetic kidney disease based on the “gut–fat–kidney” axis. International Urology and Nephrology, 1-11.

[10] Huang, L., Wu, W., & Wang, X. (2024). Analysis of the microecological mechanism of diabetic kidney disease based on the theory of “gut–kidney axis”: A systematic review. Open Life Sciences, 19(1), 20220909.

[11] Huang, H. W., & Chen, M. J. (2024). Exploring the preventive and therapeutic

mechanisms of probiotics in chronic kidney disease through the gut–kidney axis. Journal of Agricultural and Food Chemistry, 72(15), 8347-8364.

[12] Dong, K. X., Zhou, R., Chen, X., Li, S. S., Sun, Q., & Yu, X. Y. (2022). A new perspective of traditional Chinese and western medicine as a potential remedy to improve intestinal flora in the treatment of chronic kidney disease. Microenviron Microecol Res, 4(1), 4.

[13] Giordano, L., Mihaila, S. M., Amirabadi, H. E., & Masereeuw, R. (2021). Microphysiological systems to recapitulate the gut–kidney axis. Trends in biotechnology, 39(8), 811-823.

[14] Cosola, C., Rocchetti, M. T., Sabatino, A., Fiaccadori, E., Di Iorio, B. R., & Gesualdo, L. (2019). Microbiota issue in CKD: how promising are gut-targeted approaches?. Journal of nephrology, 32, 27-37.

[15] Hsu, C. N., & Tain, Y. L. (2022). Chronic kidney disease and gut microbiota: what is their connection in early life?. International Journal of Molecular Sciences, 23(7), 3954.