Dear Prof. Ma,

Thank you very much for considering our article to be published in the World Journal of Diabetes and for your advice in order to enhance the manuscript. We are also truly grateful to the reviewers and the science editor for their constructive help.

Please, let the reviewers and the science editor know our gratitude for their comments and suggestions that have greatly improved our manuscript. We are deeply grateful for the time and effort they devoted to enrich the article.

Please, kindly find here the amendments we have made following your and their recommendations.

A. Reviewer #1:

1. The manuscript cites appropriately the important and authoritative references in the introduction and discussion sections, but missing some important new references. Examples:
Paunas FTI, Finne K, Leh S, Osman TA, Marti HP, Berven F, Vikse BE. Characterization of glomerular extracellular matrix in IgA nephropathy by proteomic analysis of laser-captured microdissected glomeruli. BMC Nephrol. 2019 Nov 14;20(1):410. doi: 10.1186/s12882-019-1598-1. PMID: 31726998; PMCID: PMC6854890.

Feng S, Gao Y, Yin D, Lv L, Wen Y, Li Z, Wang B, Wu M, Liu B. Identification of Lumican and Fibromodulin as Hub Genes Associated with Accumulation of Extracellular Matrix in Diabetic Nephropathy. Kidney Blood Press Res. 2021;46(3):275-285. doi: 10.1159/000514013. Epub 2021 Apr 22. PMID: 33887734 3.

These two references have been incorporated.

2. The MS can be improved by elaborating on the biochemical methods used in discovery of the ECM composition. It will also add value if authors discussed the pathways regulating ECM synthesis and abnormalities.

We have thoroughly search Reference Citation Analysis and PubMed again. The following articles have been revised and a summary of some of them has been added to the review.

Rosso et al. 2004
From cell-ECM interactions to tissue engineering

Marastoni et al. 2008
Extracellular matrix: a matter of life and death

Daley et al. 2008
Extracellular matrix dynamics in development and regenerative medicine

Junglas et al. 2009
Connective tissue growth factor induces extracellular matrix deposition in human trabecular meshwork cells

Villareal et al. 2011
Coordinated regulation of extracellular matrix synthesis by the microRNA-29 family in the trabecular meshwork

Tovar-Vidales et al. 2011
Transforming growth factor-beta2 utilizes the canonical Smad-signaling pathway to regulate tissue transglutaminase expression in human trabecular meshwork cells

Lu et al. 2011
Extracellular matrix degradation and remodeling in development and disease

Ozbek et al. 2010
The evolution of extracellular matrix

Keely P. 2011
Mechanisms by which the extracellular matrix and integrin signaling act to regulate the switch between tumor suppression and tumor promotion

Schedin and Keely. 2011
Mammary gland ECM remodeling, stiffness, and mechanosignaling in normal development and tumor progression

Schiller and Huster 2012
New methods to study the composition and structure of the extracellular matrix in natural and bioengineered tissues

Riemer et al. 2012
Determination of the glycosaminoglycan and collagen contents in tissue samples by high-resolution 1H NMR spectroscopy after DCl-induced hydrolysis

Maquart and Borel. 2012 (abstract)
[50 years of connective tissue research: from the French Connective Tissue Club to the French Society of Extracellular Matrix Biology]

Lan HY. 2012
Transforming growth factor-β/Smad signalling in diabetic nephropathy

Lan and Chung 2012
TGF-β/Smad signaling in kidney disease

Gehler et al. 2013

Bi-directional signaling: extracellular matrix and integrin regulation of breast tumor progression

Li et al. 2013
The microRNA miR-433 promotes renal fibrosis by amplifying the TGF-β/Smad3-Azin1 pathway

Villareal et al. 2014
Canonical wnt signaling regulates extracellular matrix expression in the trabecular meshwork

Halper and Kjaer 2014
Basic components of connective tissues and extracellular matrix: elastin, fibrillin, fibulins, fibrinogen, fibronectin, laminin, tenascins and thrombospondins

Gattazzo et al. 2014
Extracellular matrix: a dynamic microenvironment for stem cell niche

Bonnans et al. 2014
Remodelling the extracellular matrix in development and disease

Badylak et al. 2015
Reprint of: Extracellular matrix as a biological scaffold material: Structure and function

Meng et al. 2015
TGF-β/Smad signaling in renal fibrosis

Rainero E. 2016
Extracellular matrix endocytosis in controlling matrix turnover and beyond: emerging roles in cancer

Chen and Liu 2016
Advancing biomaterials of human origin for tissue engineering

Riis et al. 2016
Mass spectrometry analysis of adipose-derived stem cells reveals a significant effect of hypoxia on pathways regulating extracellular matrix

Theocharis et al. 2016
Extracellular matrix structure

Schaefer and Reinhardt. 2016
Special issue: Extracellular matrix: Therapeutic tools and targets in cancer treatment

Huang et al. 2017
The Challenge in Using Mesenchymal Stromal Cells for Recellularization of Decellularized Cartilage

Holle et al. 2018
Cell-Extracellular Matrix Mechanobiology: Forceful Tools and Emerging Needs for Basic and Translational Research

Leonard et al. 2018
Methods for the visualization and analysis of extracellular matrix protein structure and degradation

Chermnykh et al. 2018
Extracellular Matrix as a Regulator of Epidermal Stem Cell Fate

Filipe et al. 2018
Charting the unexplored extracellular matrix in cancer

Skhinas and Cox 2018
The interplay between extracellular matrix remodelling and kinase signalling in cancer progression and metastasis

Chen et al. 2018
Central role of dysregulation of TGF-β/Smad in CKD progression and potential targets of its treatment

Li et al. 2018
TGF-β-mediated upregulation of Sox9 in fibroblast promotes renal fibrosis

Chen et al. 2018
Central role of dysregulation of TGF-β/Smad in CKD progression and potential targets of its treatment

Boppart and Mahmassani 2019
Integrin signaling: linking mechanical stimulation to skeletal muscle hypertrophy

Hastings et al. 2019
The extracellular matrix as a key regulator of intracellular signalling networks

Li et al. 2019
Upregulation of HER2 in tubular epithelial cell drives fibroblast activation and renal

Manou et al. 2019
The Complex Interplay Between Extracellular Matrix and Cells in Tissues

Bergholt et al. 2019
Raman Spectroscopy: Guiding Light for the Extracellular Matrix

Theocharis et al. 2019
The extracellular matrix as a multitasking player in disease

Wen et al. 2020
Decreased secretion and profibrotic activity of tubular exosomes in diabetic kidney disease

Li et al. 2020
Inhibiting Rab27a in renal tubular epithelial cells attenuates the inflammation of diabetic kidney disease through the miR-26a-5p/CHAC1/NF-kB pathway

Ding et al. 2020
Effect of cell-extracellular matrix interaction on myogenic characteristics and artificial skeletal muscle tissue

Gerarduzzi et al. 2020
The Matrix Revolution: Matricellular Proteins and Restructuring of the Cancer Microenvironment

Winkler et al. 2020
Concepts of extracellular matrix remodelling in tumour progression and metastasis

Elagamey et al. 2020
Extracellular Matrix Proteome: Isolation of ECM Proteins for Proteomics Studies

Assunção et al. 2020
Cell-Derived Extracellular Matrix for Tissue Engineering and Regenerative Medicine

Sherlock et al. 2021
Biophotonic tools for probing extracellular matrix mechanics

Li et al. 2021
Identification of Hub Genes and Potential ceRNA Networks of Diabetic Nephropathy by Weighted Gene Co-Expression Network Analysis

Karamanos et al. 2021
A guide to the composition and functions of the extracellular matrix

Halper J. 2021
Basic Components of Connective Tissues and Extracellular Matrix: Fibronectin, Fibrinogen, Laminin, Elastin, Fibrillins, Fibulins, Matrilins, Tenascins and Thrombospondins

Assunção. 2021
Hyaluronic acid drives mesenchymal stromal cell-derived extracellular matrix assembly by promoting fibronectin fibrillogenesis

Chiang et al. 2021
Bioactive Decellularized Extracellular Matrix Derived from 3D Stem Cell Spheroids under Macromolecular Crowding Serves as a Scaffold for Tissue Engineering

Zhu et al. 2021
Cell-derived decellularized extracellular matrix scaffolds for articular cartilage repair

Feng et al. 2021
Microgel assembly: Fabrication, characteristics and application in tissue engineering and regenerative medicine

Wang et al. 2022
Application of weighted gene co-expression network analysis to identify novel key genes in diabetic nephropathy

Kim et al. 2022
Kidney Decellularized Extracellular Matrix Enhanced the Vascularization and Maturation of Human Kidney Organoids

Wilks et al. 2022
Quantifying Cell-Derived Changes in Collagen Synthesis, Alignment, and Mechanics in a 3D Connective Tissue Model

Zhao et al. 2022
Talin-1 interaction network in cellular mechanotransduction (Review)

Yanes and Rainero. 2022
The Interplay between Cell-Extracellular Matrix Interaction and Mitochondria Dynamics in Cancer

Feiteng et al. 2022
Relaxin inhibits renal fibrosis and the epithelial-to-mesenchymal transition via the Wnt/β-catenin signaling pathway

Krepinsky JC 2022
Activin B, a new player in kidney fibrosis?

Sun et al. 2022
Tubule-derived INHBB promotes interstitial fibroblast activation and renal fibrosis

Serag et al. 2022
Renoprotective effect of bone marrow mesenchymal stem cells with hyaluronic acid against adriamycin- induced kidney fibrosis via inhibition of Wnt/β-catenin pathway

B. Reviewer # 2

1. I have not found that you have mentioned α3β1, α2β1, α5β1 and αvβ3 integrins which are described in scientific literature as mediators for collagen IV. Their expression differs in

high and normal glucose concentrations. Can you explain? I recommend mentioning its role if necessary.

The following articles involving integrins were reviewed and added to the article: Aggeli et al. 2009, Kitsiou et al. 2003, Karamessinis et al. 2002, Kretzler M 2002, Krishnamurti et al.1996, and Grenz et al. 1993

The role of integrins in the normal composition of the kidney extracellular matrix (ECM) and in patients with diabetic kidney disease (DKD) has been added in the two separate sections of the manuscript. Their interaction with type IV collagen and their different expression according glucose concentration have been particularly included. A figure (figure 3) has been added.

2. I have not found that you have mentioned integrin-linked kinase (ILK)

The following articles were reviewed: Górska and Mazur 2022, Xu et al. 2017, Kim et al. 2013, Woroniecka et al. 2011, Yan et al. 2010, Blattner and Kretzler 2005, Li et al. 2003, Guo et al. 2001, Guo and Wu 2002, Zhang et al. 2002, Wu C 2004, Yang et al. 2005, Sepulveda and Wu 2006, Kim et al. 2007, and Jung et al. 2007, and some of them were incorporated to the article in the two sections.

3. I have not found that you have mentioned PINCH

The following articles were reviewed: Yang et al. 2021, Kim et al. 2015, Ghatak et al. 2013, Randriamboavonjy et al. 2012, Kovalevich et al. 2011, Wickström et al. 2010, Yang et al. 2009, Chiswell et al. 2008, Li et al. 2007, and Velyvis et al. 2001, and some of them were added to the review.

4. I have not found that you have mentioned CH-ILKBP (calponin homology domain-containing ILK binding protein)

Two articles were reviewed (Tu et al. 2001 and Fukuda et al. 2003) and included in the review. We could not find more relevant articles regarding the role of CH-ILKBP in DKD.

5. I have not found that you have mentioned matrix metalloproteinases (MMP) and tissue inhibitor of metalloproteinase (TIMP) which are involved in basement membrane turnover. Can you explain? I recommend mentioning its role if necessary.

The following manuscripts were reviewed: Yu et al. 2021, Enoksen et al. 2021, Zuo et al. 2021, Liu et al. 2020, Stabouli et al. 2020, Guvercin et al. 2018, Afkarian et al. 2015, Altemtam et al. 2012, Liu and Wu 2006, Aggeli et al. 2009, Kitsiou et al. 2003, Karamessinis et al. 2002, Peeters et al. 2018, Vilmi-Kerälä et al. 2017, Peeters Engelen Buijs Chaturvedi Fuller Jorsal 2017, Peeters Engelen Buijs Jorsal Parving Tarnow 2017,

Peeters et al 2015, Macgregor et al. 2009, Ishikawa et al. 2008, Głowińska-Olszewska and Urban 2007. Not all of them were included to avoid excessive repetition of information.

6. I have not found that you have mentioned TGF-β, which increased expression is linked with increased expression of matrix components in diabetic nephropathy. Can you explain? I recommend mentioning its role if necessary.

We reviewed the following articles regarding TGF-β: Metwally et al. 2005, Ibrahim and Rashed 2007, Hills and Squires 2011, Dey et al. 2012, Shaker and Shadik 2013, Vasanthakumar et al. 2015, Chang et al. 2016, Mou et al. 2016, Voelker et al. 2017, Qiao et al. 2017, Zhou et al. 2018, Maity et al. 2020, Capelli et al. 2020, and Zhang et al. 2021
The role of TGF-β has been mentioned in the two sections of the article (normal kidney and DKD)

7. I have not found that you have mentioned growth factors such as PDGF. Can you explain? I recommend mentioning its role if necessary.

Concerning PDGF the following articles were evaluated: Kok et al. 2014, Seikrit et al. 2012, Osterdorf et al. 2012, Nakawaga et al. 2012, Osterdorf et al. 2011, Floege et al. 2008, Van Roeyen et al. 2006, and Uehara et al. 2004

The impact of PDGF on the composition of kidney ECM in normal subjects and patients with DKD has been integrated.

8. I have not found that you have mentioned growth factors such as VEGF. Can you explain? I recommend mentioning its role if necessary.

The following articles were read: Barc et al. 2021, Majumder and Advani 2017, Moriya and Ferrara 2014, Warren et al. 2014, Mironidou-Tzouveleki et al. 2011, Eremina et al. 2008 Zhu et al. 2007, Baelde et al. 2007, Sartelet et al. 2005, Foster et al. 2003, Bortoloso et al. 2001, Larrivee and Karsan 2000, Hoving et al. 2000, Thomas et al. 2000, and Simon et al. 1995. Not all of them were included, but the role of VEGF was explained.

9. I have not found that you have mentioned transcription factor NF-κB, which expression is increased in diabetic patients in proximal tubular epithelial cells. Can you explain? I recommend mentioning its role if necessary.

The following articles were examined: Kopitek et al. 2021, Deng et al. 2021, Sahukari et al. 2020, Zhang et al. 2019 (abstract), Meyerovich et al. 2018, Panday et al. 2016, Bae et al. 2011, Zhong et al. 2011, and Zhao et al. 2011. We briefly mentioned the potential role of this transcription factor on kidney ECM composition in patients with DKD.

10. I have not found that you have mentioned advanced glycation end-products (AGE). Can you explain? I recommend mentioning its role if necessary.

The following articles concerning advanced glycation end-products (AGE) and their receptors were read: Tanji et al. 2000, Heidland et al. 2001, Wendt et al. 2003, Jensen et al. 2005, Bohlender et al. 2005, Suzuki et al. 2006, Busch et al. 2010, Daroux et al. 2010, and Peeters et al. 2018. The potential role of AGEs in DKD has been mentioned.

11. Glomerular extracellular matrix (GEM) and glomerular basement membrane (GBM) are puzzling researches for few decades now and we can find many in vitro researches and review articles describing this topic. Therefore, in order to add more value to scientific literature your review article should be more comprehensive and summarize majority of data for this complex topic that we know for now. I recommend to do additional research on this topic, particularly more recent review articles, and add more data which are lacking to further increase the quality of your work.

We did additional research for recent review articles on the topic. The following recent review articles were read: Górska Mazur 2022, Viana et al. 2022, Lan et al 2022, Zhang et al. 2021, Naylor et al. 2021, Zhao et al. 2021, Liu et al. 2020, Hobeika et al. 2017, and Yan et al. 2010. We could not find more review articles regarding kidney ECM composition after thoroughly searching PubMed. Not all of them were included in our manuscript to avoid repetition of information.

12. I recommend adjusting the manuscript style according to the Baishideng Publishing Group Inc. requirements (e.g., key words, brackets, titles, subtitles, references, etc.). You can check previous review articles published in the World Journal of Diabetes.

The manuscript has been adjusted to the Baishideng Publishing Group Inc. requirements after checking authors´s instructions and previous review articles published in the World Journal of Diabetes.

13. Table 1, line Other components does not fit in the Table composition. If other components are added with unknown presence in GBM and Mesangial matrix this should be formatted to suite Table composition.

Table 1 has been modified according to the reviewer´s indications.

14. Figure 3 is unclear. Is it showing variations in some components of the glomerular extracellular matrix by the stage of DKD (earlier vs. later stage)? If so this should be explained and I suggest adding abscissa (x-axis) describing change in components.

Yes, the figure attempted to show variations in some components of the glomerular ECM according to the stage of DKD (earlier vs. later stage). We are sorry it did not work properly. We have made amendments in the figure trying to make it clearer.
We did attempt the addition of an abscissa axis, but it proved difficult because the changes in the components are not in the same direction.

C. Editorial Office's comments

(1) Science editor:
This review described the current knowledge on the biochemical composition of the glomerular extracellular matrix in patients with diabetic kidney disease. It is a invited manuscript and is well written. However, the manuscript still has some minor problems that can be further improved. 1. Missing some important new references. 2. No critiques or pros and cons of other researchers' findings. 3. Overall, this manuscript seems not comprehensive enough. The author can refer to the reviewer's comments to do additional research and add more data to fulfil their manuscript. 4. Table 1 and Figure 3 need to be revised. 5. The Author contributions and Core tip parts are missing. 6. The reference type should follow the requirements of Baishideng Publishing Group Inc. 7. please provide documents following the requirements in the journal's Guidelines for manuscript type and related ethics: （1）Conflict-of-Interest Disclosure Form；（2）Copyright License Agreement.

Reference Citation Analysis and PubMed have been searched again for relevant information and significant articles have been incorporated (67 new references). Table 1 and figure 3 have been corrected. Author contributions and core tip have been added. The reference type has been changed. Conflict of interest disclosure form and Copyright License Agreement have been incorporated.

(2) Company editor-in-chief:
I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Diabetes, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please be sure to use Reference Citation Analysis (RCA) when revising the manuscript. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. For details on the RCA, please visit the following web site: https://www.referencecitationanalysis.com/. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the

following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list.

Reference Citation Analysis has been used. Hobeika et al. 2017, Paunas et al. 2019, Lennon et al. 2014, and Tamsma et al. 1994 are examples of refences found in Reference Citation Analysis. Figures and tables have been modified according with the indications given. Figures are original and "Copyright ©The Author(s) 2022" has been added as indicated.

Sincerely,

M. Adeva