Research on Gut-kidney Axis Regulation of Diabetic Kidney Disease Based on Multi-omics and Bacterio-drug Interaction Control Mechanism

Informed Consent

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Research Unit: The First Affiliated Hospital of Hunan university of Traditional Chinese Medicine

Department: Endocrinology, Nephrology

Informed Consent - Informed Communication Page

Dear Fellow Subjects:

You are invited to join an observational scientific study funded by the National Natural Science Foundation of China (NSFC), led by Prof. Yu Rong and conducted by the Department of Endocrinology and Nephrology. This invitation is extended to you either as a healthy individual or if you have been diagnosed with diabetes, diabetic kidney disease, or chronic kidney disease by your doctor.

Before deciding, please read the following details carefully. It will clarify the study's purpose, procedures, and duration. You'll also learn about potential benefits, risks, and discomforts. You may discuss this with your family, friends, or doctor to make an informed choice. Your participation is voluntary, and we'll safeguard your rights and interests in line with laws, regulations, and ethics.

Introduction to the study

1.Background and purpose of the study

Diabetic kidney disease (DKD) is characterized by high prevalence, multiple pathogenic mechanisms, and a lack of effective treatment and management strategies. Early detection helps to overcome treatment inertia and achieve timely medical intervention to maximize preservation of renal function in diabetic patients, which is crucial to avoid renal failure and improve clinical outcomes.The gold standard for diagnosis of DKD is renal biopsy, which has the highest accuracy. However, due to the traumatic nature of renal biopsy, low patient acceptance, the application scenario is not universal, and it is only used in cases where diabetic nephropathy is difficult to distinguish from non-diabetic nephropathy, and is not the preferred diagnostic method for DKD. In the past decade, with the emergence and application of multi-omics technologies such as metabolomics, proteomics, genomics, etc., more and more studies have recognized the prominent role of gut flora dysbiosis and gut-derived metabolites in the development of DKD.

The objective of this study is to investigate the potential risk factors associated with the development of diabetic nephropathy and explore the role of intestinal flora and metabolites in this process. The objective of the study is to examine the correlation between metabolite factors and diabetic nephropathy. The findings will provide scientific evidence for the early diagnosis of diabetic nephropathy and the prevention of this condition. Additionally, the study will identify potential strategies for the prevention and management of DKD.

The study will be conducted at the First Affiliated Hospital of Hunan University of Traditional Chinese Medicine, with an anticipated participation of over 700 subjects.

The study has been reviewed by the Ethics Committee of the First Affiliated Hospital of Hunan University of Traditional Chinese Medicine and has been deemed to comply with the principles set forth in the Declaration of Helsinki and with the standards of medical ethics.

2. Who should not participate in the study

If any of the following conditions apply to you, it would not be suitable for you to participate in this study at present: having had an infection or other acute illness episode within the last 1 month;

being exposed to systemic antimicrobial drugs or having participated in a clinical trial study of another drug within the last 3 months; having another unstable chronic disease; or having a history of acute or chronic gastrointestinal disease, such as acute gastroenteritis, functional gastrointestinal disease, inflammatory bowel disease, celiac disease, or other chronic gastrointestinal disease. We sincerely regret this exclusion but it is necessary to ensure the integrity and safety of the research.

3. What you will need to do if you participate in the study

(1) This is a single observational study that does not involve follow-up. Before you are enrolled in the study, the physician or investigator will determine whether you meet the inclusion criteria. This will be done by asking about and recording your medical history, as well as obtaining your previous hospital test results and medical records. It is important that you provide accurate and complete information to assist in this assessment.

(2) If you meet the necessary inclusion criteria, the attending physician or investigator will ask about and record your medical history, current presenting symptoms, perform tongue and pulse assessment, and collect other relevant information.

As a subject, you will be asked to cooperate with the following procedures:

① Provide samples of blood, urine, stool, and tongue. The blood sample collection will involve intravenous blood collection.

②Undergo physical and chemical tests, which include routine blood tests, fasting blood glucose tests, glycosylated hemoglobin tests, glycosylated serum protein tests, liver and kidney function tests, blood lipid tests, and urine routine tests.

The remaining samples will be used for metabolomic and bacterial flora analysis. Based on the results of these tests, further related research will be carried out.

(3) Additional matters requiring your cooperation:

To participate in this clinical study, you are kindly requested to arrive at the hospital at the specific time arranged and agreed upon with your physician or investigator for the enrollment process. It is essential that you cooperate fully with the sample collection procedures.

Please be assured that this study will not disrupt or modify your existing regular treatment plan. You are strongly recommended to adhere to the medication regimen prescribed by your doctor without any alteration.

Your participation in these procedures is an important part of this research. We will ensure that all procedures are carried out in accordance with ethical and safety standards, and your rights and interests will be protected throughout the study.

4. Possible benefits of participating in the study

By participating in this study, you will help us achieve the following objectives:

(1)Your current condition will be evaluated in a more objective and comprehensive way, which will directly contribute to establishing a more precise foundation for your clinical treatment. This means that the insights gained from this research could potentially lead to more personalized and effective treatment approaches tailored to your specific needs.

(2)You will receive complimentary consultation services regarding type 2 diabetes, type 2

diabetic nephropathy, and chronic kidney disease. These consultations can offer you in-depth knowledge and understanding of your condition, as well as provide you with the opportunity to ask questions and gain valuable advice from our expert team.

(3) Most importantly, your active involvement will play a crucial role in driving the progress of research focused on the early diagnosis, identification, and prevention strategies for Diabetic Kidney Disease (DKD). This could ultimately lead to the discovery of new and improved methods for detecting DKD at its earliest stages, identifying potential risk factors more accurately, and developing more effective preventive measures. In the long run, this may not only benefit patients like you in the future but also have a significant impact on the medical community's ability to manage and combat this disease.

5. Possible risks and discomforts, inconveniences of participating in the study

When participating in this study, you should be aware of the following possible inconveniences:

(1) Sample collection: The study requires various samples such as blood, urine, stool, and tongue samples. The collection methods are complex to ensure sample quality, which may take extra time and attention.

(2)Time commitment: You need to come to the hospital at scheduled times for enrollment and sample collection, which may disrupt your normal routine and require you to arrange your time.

(3)Information disclosure: Although we'll protect your privacy, some medical information may be disclosed within the study. We'll limit access and use following ethical and legal guidelines.

Your participation is voluntary. We'll do our best to make the process smooth and ensure the study's success.

6. Related expenses

You will only need to bear the transportation expenses for coming to the medical facility for enrollment and testing.

The subject group will pay for any study-related tests during participation and either waive or pay the study-related (endocrinology or nephrology) registration fee on enrollment day.

In case of trial-related injury or illness, the subject group is responsible for all associated medical expenses.

If you have a concurrent comorbidity, the treatment and tests for other medical conditions will not be free of charge.

7. Is personal information confidential?

Your personal information will be protected as follows:

(1) All your medical records related to this study, such as the study chart/CRF, laboratory results, and other relevant data, will be stored securely and confidentially at the hospital. The physician or researcher will record laboratory test results on your case report form.

(2)Only the physician or investigator and the Ethics Committee will have access to your medical records.

(3)When the study findings are publicly reported, your identity will not be disclosed. We will

adhere to legal requirements to ensure the confidentiality of your personal medical information.

(4)There is a possibility that your medical records, test results, and remaining samples may be used in future studies. However, you have the right to indicate now if you do not consent to such use in other studies.

8. How to get more information?

You are entitled to pose any inquiries regarding this study at your convenience. The doctor or investigator involved will furnish you with a contact number for the express purpose of addressing such queries.

In the event that you harbor any apprehensions concerning your participation in the study, you may contact the Ethics Committee office at 0731 - 85600565.

The doctor will ensure timely notification to you if any substantial new information arises during the course of the study that could potentially impact your decision to sustain your participation.

9. Voluntary option to participate and withdraw from the study

Your participation in this study is completely voluntary. You have the right to decline participation or withdraw at any point during the study without any negative impact on your relationship with your doctor or your entitlement to medical or other benefits.

Your doctor or the investigator may discontinue your participation at any time if it is deemed in your best interest. Additionally, if your test results or newly diagnosed medical condition render continued participation unsuitable, your study participation may be terminated.

If your doctor considers it necessary, you may be required to undergo laboratory tests and a physical examination. This is crucial for safeguarding your health.

10. What to do now?

Participation in this study is a personal choice. You may consult with your family or friends before deciding.

Before making a decision, it is advisable that you ask your physician or the investigator any questions you have until you fully understand the study.

We appreciate your attention to this information. If you decide to participate, please inform your physician or investigator, and they will make the required arrangements.

Please keep this document for future reference.

Informed Consent - Consent Signature Page

Clinical Research Project Title: Study on Gut-kidney Axis Regulation of Diabetic Kidney Disease Based on Multi-omics and Bacterio-drug Interaction Control Mechanism and Interventional Effect of Traditional Chinese Medicine in Treating "Spleen Failure to Disperse Essence and Poison Damage Kidney Collateral"

Ethical Review Approval Number: Ethics Committee of the First Affiliated Hospital of Hunan University of Traditional Chinese Medicine (HN-LL-KL-2021-035-01)

Consent statement:

I have read the aforementioned description of this study and have had the opportunity to discuss and inquire about this study with my physician. All queries were addressed to my satisfaction.

I am aware of the possible risks and benefits of participating in this study. I understand that participation in the study is voluntary and I confirm that I have had sufficient time to think about this and understand:

- I can ask my doctor for more information at any time.
- I can withdraw from this study at any time without discrimination or retaliation, and that my medical treatment and rights will not be affected.

I am equally aware that if I withdraw from the study, especially if I am withdrawn from the study due to medication, it would be beneficial to me and to the study as a whole if I informed my doctor of the change in my condition and completed the appropriate physical and physical-chemical examinations.

Should I require additional medication due to a change in my condition, I will seek counsel from my physician beforehand or, in the event of such a change, inform him or her of the change in a truthful manner.

I consent to access to my research data by the drug regulatory authority, ethics committee or sponsor's representative.

I agree ☐ or refuse ☐ to have my medical records and pathology specimens utilized for research other than this study.

I will be provided with a signed and dated copy of the informed consent form.

Finally, I have decided to agree to participate in this study.

Patient's signature: _____ Date:_____

Patient's contact number:_____ Mobile phone :_____

I confirm that the details of this trial have been explained to the patient, including his/her rights and the possible benefits and risks, and that he/she has been given a copy of the signed informed consent form.

Doctor's signature:_____ Date:_____

Doctor's working number: _____ Mobile phone :_____

Contact numbers of the Ethics Committee Office of the First Affiliated Hospital of Hunan University of Traditional Chinese Medicine and the department where subjects complained: 0731-85600565