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Monograph



Xiang-mei Chen, *medical doctor, chief physician, professor, an academician of Chinese Academy of Engineering. She is the president of PLA General Hospital Kidney Disease Specialist Hospital, the academic leader of National Key Disciplines of Kidney Disease. She is also the Councilor of the Asia Pacific Society of Nephrology, the president of the Chinese Society of Nephrology, the chief editor of the Journal of Chinese Society of Nephrology, and the standing vice president of the Chinese Society of Integrative Medicine.*

Editorial note: *This special article written by Academician Xiang-mei Chen and her coauthor tells the readers that the researchers in Chinese nephrology have already finished or are in the process of research and development of the following new types of diagnostic and therapeutic techniques: a noninvasive marker for diagnosis of IgA nephropathy, a novel type of biological artificial kidney that can mimic renal physiological function, a device for adsorption of myoglobin for treatment of crush syndrome and rhabdomyolysis, and a study on treatment of renal diseases with adult stem cell that has already been in clinical trial.*

Progress of translational medicine in promoting diagnosis and treatment of renal diseases

Xiang-mei Chen*, Li Zhang

State Key Laboratory of Kidney Disease, Institute and Key Laboratory of Nephrology of the General Hospital of Chinese People's Liberation Army, Beijing 100853, China

Translational medicine, a new concept put forward in the last 10 years, has been designed to have the results of basic research in medical biology quickly and effectively translated into theories, techniques, methods and drugs which can be applied in the clinical practice[1-3]. It is a feedback loop research system from basic research to clinical applications, and from clinical application to basic research, advocating cross-disciplinary collaborations[4,5]. Nephrologists in China have always been emphasizing combination of clinical and basic work, and have proposed a model composed of finding problems from clinical work, conducting in-depth basic research, and then translating basic research results into clinical application. Translational medicine model has, to a higher degree, emphasized the interdisciplinary collaborations, and the rapid transformation of basic research achievements, which will further motivate the development of early diagnosis methods of kidney diseases, new molecular targets for drug therapies, as well as characteristic treatment techniques.

1 Translational medicine promoting early diagnosis and treatment of kidney diseases

Translational medicine is an era product of biomedical development, particularly genomics, proteomics and bioinformatics development. Biomarker research is a key part of it. Not only can the development of biological databases provide important information and tools for parsing complex pathological and physiological processes, but also can a variety of biological markers obtained and screened through basic research directly serve for early warning of diseases,

* Correspondence: Xiang-mei Chen E-mail: xmchen301@126.com

clinical diagnosis, molecular typing, treatment and prognosis assessment, or even development of new drugs. IgA nephropathy is the most common chronic glomerulonephritis in China, whose diagnosis currently depends on renal biopsy diagnosis, which is not suitable for early diagnosis and multiple use as an invasive examination method. Therefore, development of non-invasive techniques for IgA nephropathy diagnosis is much-needed. We have used a method of magnetic bead separation system combined with matrix-assisted laser desorption ionization-time of flight mass spectrometry in studying peptides in urine of patients with IgA nephropathy, and have identified that the m/z1913.14 peptide (urine calmodulin peptide) can be used as a non-invasive index for diagnosis of IgAN [6].

2 Development and clinical use evaluation of new blood purification materials and equipments

Epidemiological surveys of chronic kidney disease in China have revealed an incidence rate of 11% to 13%, inferring that there are at least more than 2 million uremic patients in China. As the Chinese hemodialysis registration data showed that about 260 thousand patients are being treated with blood purification in China, most patients have failed to receive the renal replacement therapy. In China, the hemodialysis machines and peritoneal dialyzate are mainly imported products leading to the high cost of renal replacement therapy. So the establishment of a production-study-research linkage mode of China-made blood purification equipment and materials will greatly increase our treatment rate of renal replacement therapy for ESRD patients, improve the prognosis of patients, and reduce the burden on the government and society. At present, the Chinese patients receiving blood purification are facing a series of issues: 5-year survival rate of less than 50%, multiple cardiovascular and other complications, poor quality of life, and low rate of social return, which remains an important issue to be solved for improving blood purification therapy in China.

To decrease the disadvantage of incomplete function of common kidney replacement therapy, Humes et al. [7] developed the bioartificial renal tubule assist device (RAD) where the renal tubular cells were grown on the polysulfone hollow fiber membrane, a better solution to the problem of hemodialysis without the reabsorption and endocrine functions of renal tubular cells, whose phase Ⅱ clinical trials have been completed, being approved by the U.S. Food and Drug Administration (FAD). However, the primary tubular cells were restricted by its limited ability to proliferate while immortalized cells could proliferate over time resulting in dysfunction of the RAD. How to effectively control the growth of seed cells, and how to perfectly simulate functions of the kidney are the key scientific problems in the development of bio-artificial kidney. We are currently developing a new type of biological artificial kidney with analog physiological functions of the kidney, and have finished the RAD device testing in accordance with the "National reporting requirements of new medical products". Crush syndrome-caused acute kidney injury is often associated with multiple organ dysfunctions, high mortality, and treatment difficulties, in the pathogenesis of which rhabdomyolysis caused the remote organ involvement including acute kidney injury, acute lung injury, endothelial injury and coagulation abnormalities, all directly related to the large production of myoglobin. We have confirmed through basic research the toxic effects of ferrous myoglobin on cells, and have accordingly developed a adsorption unit targeting myoglobin. Pre-clinical studies are currently underway to further optimize the adsorption materials and complete the relevant technical specifications testing. If it could be studied in clinical trials, and ultimately put into clinical application, it will help solve the problem of rhabdomyolysis without specific treatment methods, and will lead to further clarification of the pathophysiological abnormalities and related mechanisms of myoglobin, truly realizing the translational medical model between basic and clinical researches through the continuous feedback, correction, perfection, and spiral going up.

3 Research on stem cell transplantation for treatment of refractory renal diseases

Stem cell research has become the most active research field of medical and even life science in which adult stem cell research is moving towards pre-clinical and clinical trials. Basic researches have confirmed the success of adult stem cell treatment in a variety of acute kidney injury models, and adult stem cell treatment is also effective in some chronic renal injury models. Currently adult stem cell therapy for kidney disease research has begun to enter into clinical trials. Sun Lingyun from the Nanjing Drum Tower Hospital, used both bone marrow mesenchymal stem cells and umbilical cord blood mesenchymal stem cells for treatment of refractory lupus patients, confirming that stem cell therapy can reduce lupus activity, improve the serum markers, and maintain stable renal function[8]. Other registered clinical trials includes the application of donor bone marrow mesenchymal stem cell therapy to treat acute kidney injury after heart surgery, application of donor bone marrow mesenchymal stem cell therapy to treat acute kidney injury caused by cisplatin chemotherapy in patients with solid tumors, and application of autolo-

gous bone marrow mesenchymal stem cells to treat patients with chronic kidney diseases. Currently a great deal of basic research results in stem cells are in urgent need of further promotion, and how to apply it to clinical treatment is a hot area of translational medicine. Although the stem cell culture techniques and the laboratory of many domestic medical institutions has been able to meet the requirements of clinical applications, our Food and Drug Administration (SFDA) has not yet officially approved adult stem cell clinical trials. The necessary premise for carrying out clinical trials of stem cell therapy includes setting up normative ethics committee review system with full protection of rights of subjects, establishing the standard operating procedures (SOP) covering the whole process of stem cell isolation, amplification, storage, transport and clinical application and the complete quality control records, strictly following the principles of scientific GCP in program design, implementation, complete and accurate data collection, scientific data analysis, and true and reliable results [9]. At present, it is an important task of the translational medical research to promote the study of stem cell clinical trials so that stem cell transplantation technology can truly become a powerful clinical tool.

4 Important impacts of sharing both biological resources library and health information resource on kidney disease research

As the basis of translational medicine, sharing of biological resources and health information resource is essential to the research of kidney disease. The importance of clinical samples resources has been widely appreciated and fully understood. Establishment of clinical genomics database integrating patient risk factors, clinical diagnosis, treatment and prognosis, and the integration of biological specimens library in patients with strict quality control, is the basic guarantee for the development of translational medicine. Strengthening the establishment of relevant ethics, law and institution, setting up of detailed operating procedures in sample collection, storage, and use, development of efficient operation, open sharing platform for cooperation, and strengthening the training and communication of related personnel, will promote the construction and perfection of kidney disease biological resources libraries in our country in order to provide effective protection for the sustainable development of translational medicine.

5 Opportunities and challenges faced by the development of translational medicine

The rapid development of translational medicine has attracted world-wide attention. The proposition of the concept of translational medicine has brought forth new requirements for the development of kidney disease-related disciplines. First, we should speed up the transformation of basic research results to clinical use; Secondly, we must strengthen the cross-disciplinary collaboration. Because of the high-speed development of modern molecular biology and bioinformatics, it is very difficult to fullfill this task by only basic scientists or clinical scientists. For translational medical research in our country, more attention should be paid to the process from clinical to basic research in order that clinicians find scientific issues and then collaborate with basic medical researchers to conduct scientific research. Thirdly, the evidence-based medical research should be strengthened. The basis of preclinical research transformation to clinical research as well as clinical practice is to conduct high-quality evidence-based medical research, where for clinical workers of our country, strengthening should be made in both philosophy, standardization of operating procedures, and construction of the talents team.

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