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Potential role of gut microbiota in kidney transplantation recipients

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Kidney transplantation (KT) is an optimal treatment for improving the survival rate and quality of life of end-stage kidney disease (ESKD) patients. Despite the recent advances in immunosuppressive treatment, immune monitoring, and strategies for various infections to which KT recipients are prone to be exposed, acute rejection remains an unresolved problem. It is known that about 10-40 % of AR still occurs within the 1st after KT even in recent years. The occurrence of early acute rejection after transplantation is associated with long-term inferior graft survival. In addition, the administration of high-dose immunosuppressants for the treatment of rejection is associated with increased mortality in KT patients by inducing infection, cancer, and cardiovascular disease. Therefore, to improve the patient's prognosis, it is very important to discriminate high-risk factors for AR development to attempt early diagnosis and proper management. Several pretransplant risk factors for AR have been demonstrated including preformed antibodies for donor's human leukocyte antigens (HLAs) or blood group antigen, the number of HLA mismatches, re-transplantation, deceased donors, black race, or gender. Knowing these has contributed to reducing AR by implementing desensitization protocols or antibody monitoring in both pre- and post-KT periods. However, these are not enough in predicting AR completely and some of them are not modifiable. Therefore, there is a need for as yet undiscovered, more specific, controllable, non-invasive biomarkers that can predict the occurrence of AR episodes. Past two decades, observational findings have demonstrated that commensal gut microbes may contribute to both human metabolic health and a variety of pathologic conditions including metabolic and immunologic diseases. In terms of KT, it is not so hard to accept the hypothesis that gut microbiota may be associated with its complications of it including AR. First, patients receiving KT are suffered from advanced chronic kidney disease or ESKD living in a uremic condition that is known to be associated with gut dysbiosis. Second, most ESKD patients have diabetes mellitus or hypertension as the cause of ESKD or bystanders both of which are well-known dysbiosis-associated cardio-metabolic diseases. Third, patients receiving KT should be exposed to many drugs that may affect gut microbiota including a variety of immunosuppressive agents and prophylactic or therapeutic antibiotics. Forth, contrariwise, dysbiosis of gut microbiota may aggravate the clinical outcomes in KT

recipients, including diarrhea, infection, and post-transplant diabetes mellitus, all of which are able to be associated with immunologic responses. Therefore, previous several studies have suggested that specific gut microbiota may be associated with AR, and more interestingly, gut-derived metabolites such as short-chain fatty acids may be involved in allograft immune tolerance. Despite the possible pivotal role of gut microbiota and its metabolites, there are only limited data supporting the potential role of gut microbiota on the complications of KT recipients. In this lecture, we will discuss the potential role of gut microbiota on allograft outcomes including AR in KT recipients.