

Glomerulus-on-a-Chip: Current Insights and Future Potential Towards Recapitulating Selectively Permeable Filtration Systems

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Abstract

Glomerulopathy, characterized by a dysfunctional glomerular capillary wall, results in proteinuria, leading to end-stage renal failure and poor clinical outcomes, including renal death and increased overall mortality. Conventional glomerulopathy research, including drug discovery, has mostly relied on animal experiments because in-vitro glomerulus models, capable of evaluating functional selective permeability, was unavailable in conventional in-vitro cell culture systems. However, animal experiments have limitations, including time- and cost-consuming, multi-organ effects, unstable reproducibility, inter-species reliability, and the social situation in the EU and US, where animal experiments have been discouraged. Glomerulus-on-a-chip, a new in-vitro organ model, has recently been developed in the field of organ-on-a-chip research based on microfluidic device technology. In the glomerulus-on-a-chip, the podocytes and endothelial cells are co-cultured in a microfluidic device with physical stimuli that mimic the physiological environment to enhance cell function to construct a functional filtration barrier, which can be assessed by permeability assays using fluorescently labeled molecules including inulin and albumin. A combination of this glomerulus-on-a chip technology with the culture technology to induce podocytes and endothelial cells from the human pluripotent stem cells could provide an alternative organ model and solve the issue of animal experiments. Additionally, previous experiments have verified the difference in the leakage of albumin using differentiated podocytes derived from patients with Alport syndrome, such that it could be applied to intractable hereditary glomerulopathy models. In this review, we provide an overview of the features of the existing glomerulus-on-a-chip systems, focusing on how they can address selective permeability verification tests, and the challenges they involved. We finally discuss the future approaches that should be developed for solving those challenges and allow further improvement of glomerulus-on-a-chip technologies

Received: June 07, 2022; **Accepted:** June 14, 2022; **Published:** June 21, 2022

Biography

Masaomi Nangaku is currently specializing in Division of Nephrology and Endocrinology.

His techniques used for studying glomerulopathy, focusing on their selective permeability verification tests.