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Development of drug efficacy testing platform for Glomerulonephritis

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Objectives: There was little evidence for the treatment of glomerulonephritis (GN), although the guideline of GN was published. Traditional in vitro and in vivo animal experiments are limited to reflect high-cost clinical trials. Therefore, we developed a new drug efficacy testing platform for GN using a 3D glomeruli tissue chip.

Methods: We designed a gravity-driven, glomerular-filtration-barrier (GFB) mimicking chip consisting of human podocytes and endothelial cells with a bi-directional flow in the bottom channel. We used the GN model induced by puromycin, a nephrotoxic drug that damages podocytes. We selected tacrolimus to evaluate drug efficacy for GN.

Results: We confirmed the expression of markers like RFP-Gendo, WT1, and nephrin as the molecular structure of the GFB. We also confirmed albumin permeability and cell viability as the function of the GFB.
WT1 and nephrin of podocytes in the GN model decreased to 70% and 50%, respectively, compared to the standard GFB model. Albumin permeability increased to 140%, and cell viability dropped to 79.4% compared to typical GFB models.
After the 6-hour administration of tacrolimus in the GN models, WT1 of podocytes in the GN model increased 1.3 times. However, the nephrin expression decreased by 20% after the same tacrolimus treatment. Albumin permeability was reduced by 22%, and cell viability was restored by 2% after the 6-hour exposure to tacrolimus in the GN models.

Conclusions: We evaluated drug efficacy using tacrolimus in the puromycin-induced GN on a chip based on the structure and function of GFB. Further research is needed to apply this platform to other GN and drugs.

Figure1. The expression of the markers as the molecular structure of the GFB