Development of a living membrane for Bioartificial Kidney Device

A key requirement for a bioartificial kidney device is the formation of a "living membrane" consisting of a tight renal cells monolayer with preserved functional organic ion transporters, on an artificial porous membrane. Recently, we showed the proof of concept of creating such living membrane using conditionally immortalized human renal proximal tubular epithelial cells (ciPTECs) [1] on polyethersulfone (PES)-based flat sheet and hollow fiber membranes [2,3]. Here, we present strategies for the upscaling of the system having several hollow fiber membranes (HFM).

HFM were mounted in modules and coated with L-Dopa and Collagen IV. The ciPTECs were seeded on the extraluminal HFM surface. The ciPTEC morphology and monolayer quality was investigated via expression of tight junction protein Zonula Occludens-1 (ZO-1)) and permeation of inulin-FITC. The functionality of organic cation transporter 2 (OCT2) was evaluated using a specific fluorescent substrate, 4-(4-(dimethylamino)styryl)-N-methyl-pyridinium iodide (ASP+), and creatinine in absence and presence of the OCT2-inhibitor cimetidine.

The upscaling of the L-dopa/CIV coating on the PES membranes was successful. After one week of culture in static conditions, reproducible cell monolayers are formed on the extraluminal side of the HFM within modules containing 3 HFM with a surface area of 4 cm^2. Furthermore, the fibers have tight and homogeneous ciPTECs monolayer formation with low leakage and optimal active transport of uremic toxins [4,5].

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