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DEVELOPMENT OF A BIOARTIFICIAL KIDNEY DEVICE FOR UREMIC TOXINS REMOVAL

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Chronic kidney disease (CKD) is a worldwide health problem. Despite the state of the art therapy, the risk of renal and cardiovascular morbidity and mortality in CKD patients remains disturbingly high. Uremic toxins, i.e. endogenous metabolites that accumulate during CKD such as indoxyl sulfate (IS) are greatly implicated in the progression of CKD as well as cardiovascular disease. Dialysis therapies do not allow the removal of these toxins, as they are often too large and highly protein bound. Hence, new treatment options call for strategies that enable the removal of these toxins. To achieve this, new therapeutical approaches are needed, such as a bioartificial kidney device (BAK).

Methods: Conditionally immortalized proximal tubules epithelial cells (ci PTEC) have been cultured on double coated (L-dopa and collagen IV) hollow fiber membranes. In order to determine the effect of healthy human serum albumin (HSA, 1 mM) and CKD-HSA (1 mM) on IS uptake, fluorescein (1 μM), an OAT-1 fluorescent model substrate, and IS 100 μM; (free and bound) uptake was performed.

Results & Conclusion: Our results show that IS (100 μM) bound to either CKD-HSA or healthy HSA slightly reduced fluorescein uptake (20.5±5.1% and 31.4±2.6% inhibition, ns, respectively) in 2D, while IS bound to healthy HSA significantly inhibited the uptake of fluo rescein by 51.7±12.5% ($p< 0.05$) in 3D. In addition, healthy HSA enhanced IS uptake in 2D by 42.4±28% ($p<0.0001$). Furthermore, both forms of albumin appeared to facilitate active IS clearance. To conclude, the presence of CKD-HSA still grants the active clearance of IS, which is essential for the eventual treatment of CKD patients using a bioartificial kidney (BAK) device. Although more research is still needed, the model here presented showed fundamental features to proceed with the development of BAK device.

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