256

A Bioreactor Containing Primary Human Renal Epithelial Cells Supported In Vivo without Immunosuppression

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Study: The bioartificial kidney is intended to contain human cells in an immunologic sanctuary and provide total renal replacement. In vitro experiments have demonstrated the efficacy of silicon nanopore membranes (SNM) as an immunologic barrier to inflammatory cytokines with selective permeability that supports human renal epithelial cell (HREC) viability. Here, we test an SNM-based bioreactor in vivo to demonstrate HREC viability and functionality without immunosuppression or anticoagulation in a swine model.

Methods: HREC were grown to confluence on semipermeable polycarbonate membranes coated with type IV collagen and separated from blood flow by SNM with 10 nm pores, allowing passage of nutrients but not immunoglobulins or immunocytes. The bioreactor was implanted in the neck of a healthy Yucatan pig for three days and perfused via anastomoses to the external jugular vein and carotid artery. A static control was comprised of HRECs grown on identical membranes in cell culture media at 37°C.

Results: HREC were evaluated for viability and biomarkers of functionality upon device explantation. Cell viability was over 90% as shown by fluorescence imaging after staining with calcein AM and ethidium homodimer-1. Cells remained confluent with tight junctions expressed by Zona Occludens (ZO1) protein comparable to that of the control. γGlutamyltransferase (γ-GT) activity, which is a renal tubule cell (RTC)-specific marker, and qPCR evaluating expression of RTC surface markers including AQP1, γ-GT, and NHE3 were consistent with healthy static control RTCs. *NAG*activity, a biomarker of RTC damage, was low. We show immunoprotection protection of primary human renal cells and preservation of renal tubule cell functional markers in a bioreactor after three-day implantation in a swine. This is a promising model for bioartificial kidney development in humans that may lead to total renal replacement.