Immunobarrier Characterization Of Slit-Shaped Nanotopography For An Implantable Bioartificial Kidney

E.J. Kim[1], W.H. Fissell[2], S. Roy[1]
[1] Department of Bioengineering & Therapeutic Sciences, UCSF
[2]Division of Nephrology and Hypertension, Vanderbilt University

Background:
Renal tubule cells are known to suffer necrosis and apoptosis after exposure to inflammatory cytokines. We are using silicon nanopore membranes (SNM) to develop an implantable bioartificial kidney that consists of a high-permselectivity hemofilter coupled with a bioreactor housing renal tubule cells. In this study, we investigated the immunoisolation function of SNM with 7 nm-wide pores by examining the effect of cytokines on epithelial tight junction of renal cells.

Methods:
Four different types of renal epithelial cells (MDCK, HK2, LLC-PK1, and HPTCs) were grown to confluence on 10 mm x 10 mm SNM substrates consisting of a central 6 mm x 6 mm slit-array patterned porous region surrounded by a 2 mm-wide smooth solid border. Transwell chambers were used as the control membranes. Human tumor necrosis factor-α (TNFα) was added to the apical side of the cells and the monolayer integrity after 6 hours of exposure was assessed via transepithelial electrical resistance (TEER), cell viability assay, and immunohistochemistry techniques.

Results:
Without TNFα, cells on both Transwell and SNM maintained the monolayer integrity by expressing zona occludens (ZO1) protein at the intercellular junctions. Regardless of cell type, TNFα broke the monolayer integrity and caused apoptosis on the apical side of cells on both Transwell and SNM. In contrast, renal cells on the basal side of the SNM maintained monolayer integrity unlike their Transwell counterparts.

Conclusions:
These results suggest that SNM provide an immunoisolation function that could be used to encapsulate renal cells in the bioreactor of the implantable bioartificial kidney.