INVESTIGATING THE POROSITY OF TRABECULAR MESHWORK USING MICROFABRICATED STRUCTURES FOR GLAUCOMA TREATMENTS

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ABSTRACT

This paper investigates the influence of microtopographies on human trabecular meshwork (TM) cells using polymer microstructures. The dependency of cell morphology on different microtopographies implies that the microfabricated surface is a viable solution for effective control of cell porosity and thus the flow resistance of human TM. This work is expected to help the treatment of open-angle glaucoma by adding insight into the regulation of intraocular pressure.

KEYWORDS: Trabecular Meshwork; Glaucoma; Microstructures; Tissue Engineering

INTRODUCTION

Primary open-angle glaucoma is one of the leading causes of blindness, affecting more than 2.25 million Americans aged 40 years and older [1]. This disease is induced by the loss of balance between the production and drainage of aqueous humour, which is secreted posterior to the iris by the ciliary body, flows to the anterior chamber, and exits the eye via TM. Many treatments of open-angle glaucoma deal with aqueous humour outflow [2-4]. Since the TM endothelial cells play an important role in the outflow facility, a better understanding of mechanisms that regulate the hydraulic resistance of TM will provide useful insights to improve the efficiency of pharmaceutical treatments.

There are several observations showing that the TM exhibit different morphologies under various physiological conditions [5,6]. According to these findings, it is plausible to deduce that the TM morphology may relate, to a certain extent, the hydraulic resistance and consequently contribute to the increase of intraocular pressure (IOP). In this study, we will examine TM cell adaptation, particularly the cell morphology, to engineering microtopography using an in vitro model.

HYDRAULIC RESISTANCE OF TRABECULAR MESHWORK

The porous TM was modeled as a solid framework made of TM cells. The flow resistance relates to the permeability $K$ expressed by Darcy’s law:

$$R = \frac{\mu L}{KA},$$

where $\mu$ is the fluid viscosity, $L$ the length of the region, and $A$ the total cross-sectional area across which the flow takes place. Since the flow resistance of the
extracellular matrix is much greater than that of the open space, we assume that the flow passes only through the open spaces. The permeability $K$ is:

$$K = \frac{\varepsilon^3}{kS^2},$$

where the Kozeny constant ($k$) depends on the pore geometry, $\varepsilon$ the porosity, and $S$ the ratio of wetted pore surface area to total volume. The relation between the flow resistance and the porosity can be found by inserting equation (2) into (1):

$$R = \left(\frac{\mu k S}{A}\right) / \varepsilon^3.$$

(3)

Therefore, while other conditions are kept constant, the flow resistance inversely relates to the porosity of trabecular meshwork.

**EXPERIMENT AND RESULT**

Two types of microtopographies (microlines and micropillars) were used. TM cells from human donor rims were cultured on these microstructures. The cell morphology was examined using diffuse cytoplasmic green fluorescence. Two common baseline cell morphologies on smooth surface topography were used: Control 1 with isotropic morphology and Control 2 with elongated morphology [7].

Trial and error experiments were performed in cell culture. Once a steady state condition for the cell volume and cell alignment were reached (after Day 6), porosity examination was performed by interposing a contrast thresholding on the optical images. The results showed that the microlines array is effective in increasing the cell porosity. For example, using Control 2 as the reference (100%), the cells cultured on microlines occupy less than 25%. Moreover, the intergroup comparison demonstrates that in single spaced microlines, high cell porosity associates with small line widths and small height-width ratios (Figure 1). The cell morphology was examined on microlines with different heights (Figure 2). Although the porosities are similar, the results show that the cells seeded on the microlines with small height-to-width ratios proliferate across the neighboring structures and have a widespread angular distribution. This may affect pore geometries and the Kozeny constant in equation (3).

The elongation degree was examined by measuring the maximum length-to-width ratio of a visual rectangular box where a single cell fit (Figure 3), suggesting that
microlines are most efficient in mimicking the *in vivo* like elongated morphology, while micropillars direct the cells into more isotropic shapes.

**CONCLUSION**

This work shows that the TM cell porosity varies with the microtopographies on which the cells are cultured. Since the cell porosity directly relates to the aqueous humor outflow facility, one may be able to regulate the hydraulic resistance by creating appropriate microtopographies. This *in vitro* model provides a promising starting point for understanding topography-based regulation of IOP, which is expected to shed light on the treatment of open-angle glaucoma.

**REFERENCES**


