Analysis of liver cell aggregate motility on synthetic polymer films: effect of void microstructure

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Introduction

The ability to control hepatocyte aggregation on synthetic polymeric substrate is crucial in cell transplantation for treatment of liver failure. In order for the the primary liver cells, hepatocytes, to function properly, it is critical that they maintain a suitable morphology on the substrate as they do in native liver. In previous studies, hepatocytes have been observed to reorganize and aggregate to varying extents on synthetic porous poly-glycolic and poly-lactic acid scaffolds; however, little is known quantitatively about such phenomena. This study focuses on identifying the effect of various degrees of surface texture of the polymeric substrates on the rate and extent of hepatocyte aggregation.

Materials and Methods

Hepatocyte aggregate motility and reorganization on 2-D surface textured polymeric films were investigated in response to a range of pore size distributions (~1 □m to ~100 □m). Thin scaffold analogs were fabricated by spin-coating 0.05 % w/v ratio solution of 50/50 D,L PGLA (Medisorb Technologies International, L.P.) in histological grade 1,4 dioxane (Fisher Scientific) on 25 mm glass/plastic coverslips and subjecting them to differential phase separation via quenching and sublimation. The transparent nature of the thin PGLA films facilitated real-time observation using time-lapse optical microscopy and digital image anlaysis. By tracking and measuring the aggregating cell populations via Image-Pro Plus (Media Cybernetics) on obtained image sequences, we calculated a mean squared displacement, $< d^2 >$. The objective random motility coefficient (□) was then computed for each type of microporous matrix, using the equation,

$$< d^2(t) >= 4\mu \bullet [t - P\{1 - \exp(-t/P)\}]$$

Results and Discussion

We have observed that hepatocyte aggregation on textured PGLA films strongly correlates with pore size. As the surface voids became smaller, hepatocyte population migrated more vigorously [Fig. 1]. Correspondingly, the random motility coefficient,

a quantitative index for cell population motility, generally increased for smaller pore size distributions, ranging from 5.0×10^{-11} to 7.86×10^{-12} cm^2/s [Fig. 2]. Thus, we conclude that the scale of the surface structure of the polymer substrate has a significant effect on hepatocellular aggregation.

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Figure 1: Mean square displacement of liver cells on polymer substrates with different pore sizes.

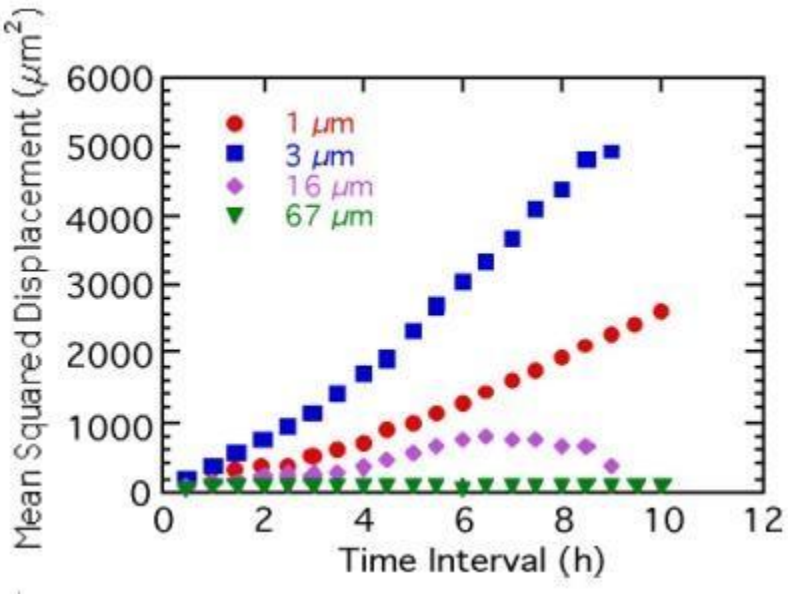

Figure 2: Population-averaged aggregation coefficient varies sensitively with polymer surface topography.