PDMS Collagen-GAG Networks with Microvasculature

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Statement of Purpose: Statement of Purpose: Currently, to address nutrient transport in tissue engineered products several strategies including porous matrices, hydrogels and angiogenic factor delivery[1] have been investigated. These approaches, however, rely primarily on passive diffusion until such a time that the product is vascularized *in vivo* through angiogenesis. A promising approach is the integration of microvascular networks within synthetic biodegradable polymers[2] prior to implantation.

The primary goal of this research is to design and develop a closed channel semi-synthetic PDMS / Collagen-GAG composite matrix with capillary flow networks having optimal mass transport characteristics (Figure 1). The PDMS adhesive layer is semi-permeable and provides control of water loss, protection against bacterial infection and increased strength to the composite membrane. The built-in endothelialized flow networks in collagen efficiently deliver nutrients and remove waste products from the TE product with minimal frictional losses. This will lead to better host integration due to enhanced vasculature and have applications in the management of skin wounds.

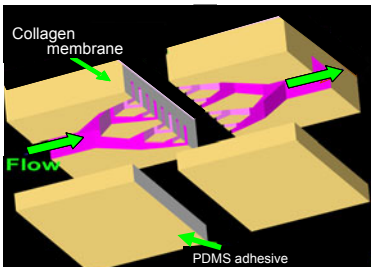

Figure 1: Schematic of a PDMS – Collagen-GAG composite microvascular network

Methods: BIO-PSA® grades 7-4601, hydroxyl terminated PDMS (PDMS-OH) in ethyl acetate solvent were obtained from Dow Corning Corp. These were solution cast on a fluorinated silicone release line and dried at 80 ^{0}C to evaporate the solvent. The thickness of the dried adhesive layer was about 38 microns (1.5 mils). Collagen-GAG membranes were fabricated by vacuum filtering a mixture of collagen and chondroitin-sulfate homogeneously suspended in 0.01 M acetic acid solution[3]. Micron dimension flow networks optimized for maximum mass transfer efficiency and minimum pressure losses were fabricated on silicon wafers using standard photolithography techniques. These microvascular networks were cast onto the collagen-GAG biopolymeric matrices using a novel collagen soft lithography technique developed in our lab. Four process parameters were optimized to obtain well-resolved and stable features: acetic acid (AA) solution concentration, surface dissolution time, applied pressure and glutaraldehyde concentration. The collagen GAG membranes adhered onto the PDMS adhesive sheet to form the composite membranes.

High resolution Scanning Electron Microscopy (SEM) was used to image a cross-section of the PDMS collagen-GAG networks. Further, the pressure drop-flow rate relationship was verified for composite networks as well as for comparable PDMS networks as a function of generations increasing from 1 to 6 (higher the generation number, greater the design complexity).

Results/Discussion: An SEM cross-sectional image of the composite network can be seen in Figure 2(a). The results show that channel gaps of thickness 100 microns

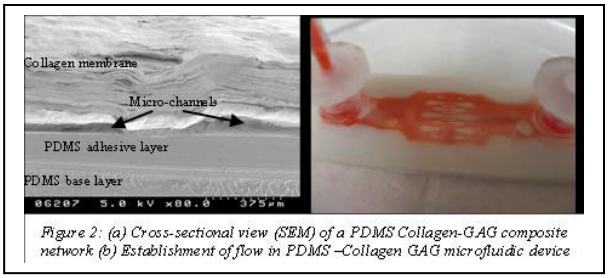

Figure 2: (a) Cross-sectional view (SEM) of a PDMS Collagen-GAG composite network (b) Establishment of flow in PDMS –Collagen GAG microfluidic device

comparable to the starting dimensions in the silicon wafer template. Microfluidics was established in the composite network by flowing a red dye through the micro-channels (Figure 2(b)). This shows that the networks are patent and

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A typical pressure drop versus flow rate curve is shown in Figure 3 for a 5th generation PDMS microfluidic device and a comparable PDMS collagen-GAG composite network. It can be observed that the frictional resistance (mmHg /ml/min) in the composite channels is about twice greater in collagen-GAG than that in the PDMS network, due to the porous nature of the material and inherent differences in the surface smoothness of the two materials.

Conclusions: We have successfully developed a composite PDMS collagen-GAG microfluidic network. The proposed design offers protection against infections and provides enhanced convective mass transport of nutrients via the capillary flow networks. It thus addresses the issue of mass transport limitations in current tissue engineering and can lead to the development of a composite permanent skin graft.

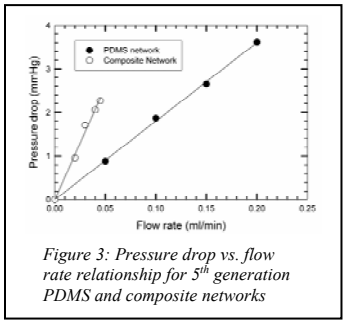

Figure 3: Pressure drop vs. flow rate relationship for 5th generation PDMS and composite networks

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1. Murphy WL. Biomaterials. 2000; 21(24): 2521-27.
2. Fidkowski C. Tissue Eng. 2005; 11(1-2): 302-9.
3. Yannas IV. J Biomed Mater Res. 1980; 14(2):107-32.