

Microstructured Immunoregulatory Scaffolds for Controlling Host-Biomaterial Interactions

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Statement of Purpose: Cytokine signaling is critical in host responses to implants but it has been difficult to control this. We present a study on the development of microstructured scaffolds that present cytokine-neutralizing antibodies to regulate cellular responses at device interfaces. The hypothesis of this research is that antibody-functionalized microstructured scaffolds can provide an immunoregulatory environment.

Methods: Rat anti-mouse TNF monoclonal antibodies (R&D Systems) were conjugated to hyaluronic acid with molecular weight 1.6 MDa (Life Technologies) using carbodiimide coupling. Adhesion to the scaffold surface was mediated by grafting poly(methoxy diethoxy methacrylate) (PMEO₂MA) to the HA, which undergoes a lower-critical solution temperature around 30 C. Laser micromachining was used to prepare scaffolds based on poly(methyl methacrylate) that were subsequently functionalized with HA-antibody.

Results: PMOEO₂MA was synthesized using atom transfer radical polymerization, and the bromine terminus was replaced with an amine for coupling to HA, as shown in Figure 1.

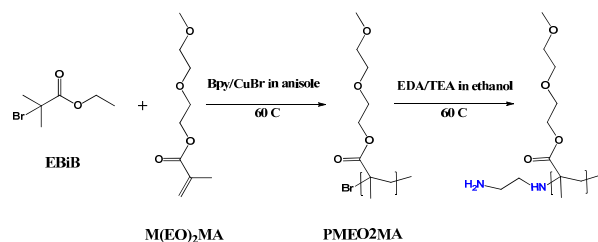


Figure 1. Synthesis of PMEO₂MA.

In Figure 2 is shown the CAD rendering of the scaffold along with a fluorescence micrograph of a microfabricated scaffold coating with fluorescently labeled HA. The field of view in the micrograph is 500 um, and 100 um features are observed.

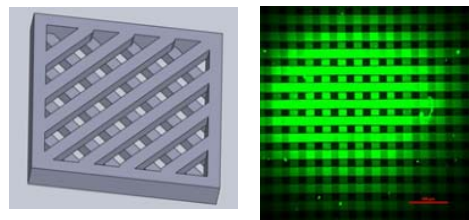


Figure 2. CAD rendering of a scaffold along with a fluorescence micrograph of a sample. Sample feature size is approximately 100 um.

Scaffolds containing antibodies against tumor necrosis factor- α have been fabricated and are being tested using a

macrophage RAW cell line containing a reporter gene construct for NF- κ B translocation.

Conclusions: Microstructured scaffolds have been prepared containing HA and cytokine-neutralizing antibodies. These may be able to control inflammatory responses at biomaterial interfaces.