Assessing Innate Immunity in Implant Biointegration Using Surface-Treated, Microporous PDMS Scaffolds

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Assessing Innate Immunity in Implant Biointegration Using Surface-Treated, Microporous PDMS Scaffolds

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In order to devise long-lived, functional implants, it is necessary that the material from which the implant derives does not conduce destructive immune responses. Innate immune mechanisms, including acute and chronic inflammation and the ensuing foreign body reaction, dictate whether or not biointegration is successful. Thus, when designing biomaterials, it is imperative to cater to known physiological processes which will not trigger undesirable immunological outcomes, but rather support healing processes. This process, called biointegration, involves a seamless physical interconnection between biomaterial and recipient tissue. Many patients who undergo implantation fail to achieve biointegration, cascading to epithelial downgrowth and bacterial infection, subsequent device failure and removal, and in rare circumstances, sepsis. With this in mind, there exists a pressing need to further optimize modern implants in order to maintain device stability, efficacy, and safety. Because the interaction of host tissue with the biomaterial occurs largely at the material surface, modulation of surface chemistry is an enticing means for improving biointegration. Here, we generated microporous, PDMS bioscaffolds with altered surface chemistries as a model to assess how well modified implants may assuage host immunity in vitro. Following surface treatment with polydopamine (PDA) alone or PDA + TiO₂—both promising surface modifications for improving implant outcome—, scaffolds were cultured with either macrophages (MΦ), dermal fibroblasts (DF), or mesenchymal stem cells (MSC) to elucidate how these surface chemistries may either promote or obstruct successful implantation. Understanding how specific surface chemistry modifications like these dictate innate immune mechanisms and wound healing processes will help inform future design of future immunomodulatory biomaterials.

Methods

PDMS Scaffold Fabrication—

Progen (Inkjet) addition to PDMS solvent

Surface Modification and Characterization—Untreated PDMS discs were immersed in a dilute, aqueous solution of dopamine (2 mg/ml dopamine in 10 mM Tris buffer, pH 8.5) for 24 h with light shaking to generate a layer of PDA. After a thorough wash with deionized water, the PDA-coated sponges were immersed in 0.1M ammonium hexafluorotitanate ([NH₄]₂[TiF₆]₂) and 0.3M boric acid ([H₃BO₃] solution at pH 3.9 overnight on a shaker at room temperature to result in TiO₂ coating.

Cell Culture and Seeding—MSCs, DF, and monocytes were cultured in T75 flasks in the proper medium, prior to seeding onto scaffolds in a 24-well plate. All cell types were incubated at 37° C in a 5% CO₂ environment. Monocytes were allowed to differentiate into MΦ for 7 days prior to seeding. Seeding densities were as follows (cells/well): MSC 5×10⁴, DF 1.9×10⁴, MΦ 1.6×10⁴.

Enzyme-Linked Immunosorbent Assay—ELISAs were performed using kits from Boster Immunoreader. For this measurement, the medium added to cells was collected from each well after 24 h. These samples were centrifuged at 1000 rpm for 5 min and the supernatant was collected for cytokine analysis. For a positive control, one set of cells (N=4) per cell type was spiked with bacterial lipopolysaccharide (LPS) at a concentration of 0.2 mg/mL.

Conclusion & Future Studies

Here, we have established a successful mechanism for generating microporous, PDMS scaffolds with altered surface chemistries—including deposition of PDA and TiO₂—as a model for characterizing success of implant biointegration. TiO₂ coating on PDMS results a marked decrease in production of the pro-inflammatory cytokine tumor necrosis factorα in macrophages, making it a suitable candidate for biomaterial modification.

In the future, a larger panel of cytokines, including those vital for both wound healing and inflammation, must be assessed. DF proliferation and adherence to these scaffolds should also be examined. Lastly, in vivo experimentation is necessary to examine overall tissue reaction to implantation.

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