

Viability of *Staphylococcus epidermidis* and Fibroblast Cells in Microscale Environments

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In many infections, bacteria attach to the surfaces of medical devices or immunocompromised tissues, and subsequently develop into highly cooperative biofilms. Biofilms interact in very complex and dynamic manners with device surfaces, host cells, and therapeutic interventions. We have designed, fabricated, and evaluated microfabricated bioreactors, which are referred to as “microreactors,” in an iterative manner for studying cell-bacteria-biomaterial interactions. Two different microreactors fabricated by micromolding of poly(dimethylsiloxane), PDMS, were used to compare and contrast the effects of microscale environments on the adhesion, growth, and dispersal behavior of biofilm-producing *Staphylococcus epidermidis* versus on the adhesion and spreading behavior of 3T3 mouse fibroblast cells.

The first microreactor contained two microscale environments: (1) a simple 25 mm long microchannel of 100 μm width and 100 μm depth and (2) two microplate areas of 2 mm x 2 mm with 100 μm depth. The second microreactor consisted of: (1) a microchannel of 200 μm width and 30 μm depth and (2) a micromixer with microfabricated valves for precise control over flow sequencing and mixing. Flow rate was controlled in the range of 5 to 50 $\mu\text{l}/\text{min}$ using a syringe pump. Biofilm development and fibroblast cell adhesion were mainly characterized by microscopic imaging and by effluent analysis.

We observed that the development of *S. epidermidis* biofilm was active in both the microreactors. Also, its morphology was strongly influenced flow rate, inoculating concentration, and the dimensions of the microscale environments. On the other hand, fibroblast cell adhesion and spreading became highly restricted by the narrow and shallow dimensions of the microchannels in comparison to Petri-dish culture results obtained from flat PDMS samples. Comparison of these observations suggested that *S. epidermidis* bacteria are more active than fibroblast cells in the 3-D microscale environments in a relative sense. We are currently developing microreactor-based co-culture procedures to dynamically monitor interactions between bacteria and eukaryotic cell interactions within the microenvironments.

The preliminary research provides an interesting basis for discerning the effects of microscale dimensions and geometries on bacteria and eukaryotic cell interactions. We think that this is an important issue since microenvironments are natural parts of human physiology and are also important parts of biomedical devices which can be proactively engineered. For example, the microenvironments emulated by our microreactors could represent small physical gaps may exist between at bone tissue and orthopaedic device surfaces during an implant surgery. From this ambitious perspective, our long-term aim is to explore the possibility of developing a more predictable *in vitro* model for orthopaedic implant infection control based on recent advances in microreactor technology.