Engineering Biomaterials to Modulate the Immune Response to Implants

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Immune cells are central regulators of wound healing, and play an important role in the host response to implanted materials. In particular, macrophages are innate immune cells that help orchestrate this response by performing a variety of functions in response to biochemical and physical cues in their microenvironment. Our laboratory seeks to better understand how microenvironmental cues regulate the behavior of macrophages in order to design better biomaterials for medical devices and tissue engineering. In one approach, we leverage the ability of immune cells to distinguish self from non-self via specific molecules expressed on the surface of host versus foreign surfaces. We found that decorating biomaterials with an endogenously expressed immunomodulatory self-antigen, CD200, inhibits macrophage activation in vitro and inflammatory cell infiltration in vivo. Current work is focused on promoting the longevity of these surfaces, and testing the effects of CD200 on biomaterials including poly(ethylene glycol) and poly(lactic-co-glycolic acid). In a complementary approach, we are engineering biomaterial surfaces with physical cues that modulate the inflammatory versus wound healing behavior of macrophages. We recently discovered that the geometry of adhesion, and specifically the elongation of macrophages promotes their polarization towards an alternatively activated, pro-healing phenotype. Elongation was synergistic with cytokines that stimulate a pro-healing response, but protected cells from inflammatory stimuli. Interestingly, surface topographies, such as grooves, that lead to changes in cell shape can also control the polarization state of macrophages, and thus influence the host response to implanted materials. Continued work focuses on better understanding the mechanism by which macrophages sense the physical microenvironment to regulate their behavior. Together, these studies aim to design materials to control the host immune response and thus improve strategies for wound healing and regeneration of tissue surrounding implanted materials.