Immune-instructive polymers for modulating macrophage polarization and promotion of wound healing

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Introduction and objectives:
Host immune responses to materials play a critical role in clinical success or failure of medical devices. Macrophages play a central role in orchestrating responses to foreign materials. A potential approach to limit these reactions is developing biomaterials with immunomodulatory abilities. These materials could direct macrophage polarisation away from pro-inflammatory phenotype and towards pro-healing phenotype, thereby accelerating wound healing and implant integration while reducing tissue damage and fibrosis. Biomaterials surface chemistry has been shown to influence macrophages function. In this study, using a high throughput screening strategy, we sought to identify immune-instructive polymers with the ability to instruct macrophage polarisation. We then assessed host response to such polymers in an in vivo model of wound healing.

Methods
A combinatorial library of acrylate or acrylamide polymers was screened to identify polymers with the ability to promote monocyte differentiation to pro (M1 like) or anti-inflammatory (M2 like) macrophages. A selection of pro or anti-inflammatory polymers were used as surface coatings for silicone implants. Immune cell infiltration, macrophage polarization, wound healing and fibrosis were studied after subcutaneous implantation of coated silicone using histology and immunohistochemistry.

Results
In this study we used a high throughput screening strategy and identified polymers that are able to support monocyte differentiation to macrophages with pro or anti-inflammatory phenotypes. We then used a selection of these plyers as coatings on silicone pieces implanted subcutaneously followed by assessing inflammatory responses and wound healing after 4 weeks of implantation. Our data show that different polymer coatings are able to change immune cell infiltration, macrophage polarization and fibrosis at the site of implant which were in line with the 'immune-instructive' function of different polymers used as coatings.

Conclusion
Our findings show that immune-instructive polymers can be used as biomaterials for fabrication of bio-instructive implants and medical devices with reduced risk of foreign body responses and enhanced functionality due to better integration and reduced fibrotic tissue formation.

Keywords : macrophages, immune modulation, immune-instructive materials, foreign body response, fibrosis
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