Title: Investigation of Macrophage Activation in Response to Nanoscale Biomaterial Surface Features

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Abstract: The control of the foreign body reaction to implanted biomaterials and tissue engineering scaffolds is a central aspect of biocompatibility. The design of biomaterial coatings that minimize chronic inflammation, yet encourage healing responses, is a key goal in the medical device field. Recent findings in this group and others have shown that materials with nanoscale fibrous features exhibit favorable in vivo biological responses. Underlying this response are differences in macrophage biology that are related to biomaterial architecture. Surface topography at small nano- to meso- scales may thus be a major influence in the biocompatibility of a material[1, 2]. With advances in genomic and proteomic technologies, it is now possible to study in unprecedented detail the pro-inflammatory activation of macrophages as a function of the nanoscale features of biomaterials. This new mechanistic detail will identify common architectural properties that can be incorporated into biomaterial surfaces. The identification of the key signaling pathway components associated with the response to nanoscale features will also provide targets for the design of drug delivery coatings from biomaterials that can augment the surface architecture effect. This collaborative proposal will combine the biomaterials and biological expertise at the University of Washington with the proteomics expertise at PNNL to study the pro-inflammatory response of macrophages to materials with nanoscale surface features. The response of human primary macrophages on polytetrafluoroethylene materials that are topographically distinct at under 100 nm will be studied using advanced techniques mass spectrometry proteomic techniques. Tandem mass spectrometry coupled with Fourier transform ion cyclotron resonance (FITCR) mass spectrometry will be used to study signaling pathway activation as monitored by phosphorylation activation of pro-inflammatory pathway components[3, 4]. The proposed research aims to characterize dynamic signaling pathways in monocyte response to better understand and control the effect of material nanostructure on the inflammatory

response.