The role of particle physico-chemical properties on phagocytosis
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Purpose: Polymeric particles are valuable carriers for drugs and vaccines due to the ability to tune their properties. When introduced into the body these particles can be rapidly cleared by macrophages through a process called phagocytosis. Studies have previously shown that particle physico-chemical properties such as size, shape and stiffness can influence phagocytosis [1-3]. However, the combinatorial effect of these physico-chemical properties on phagocytosis is still unknown. Our objective in this work is to understand how the combinatorial effects of particle physico-chemical properties size, shape and stiffness affect the process of phagocytosis using particles which can be independently tuned in each of these properties while keeping the chemistry constant.

Methods: Tunable particles have been fabricated by the development of a template based layer-by-layer (LbL) assembly process. Polystyrene spherical particles of a particular size were chosen as the template. Shape has been imparted to the templates by heat liquefaction while stretching. The template particles were adsorbed with polyelectrolytes poly (vinyl pyrrolidone) (PVP), poly (ethyleneimine) (PEI), and poly (acrylic acid) (PAA) by LbL self assembly. Mechanical stiffness has been varied by making the particles hollow through tetrahydrofuran removal of the polystyrene core and thiol crosslinking of the polyelectrolyte layers. To enable specific Fc receptor interaction and monitor their interaction with macrophages, the particles were coated with IgG and made fluorescent. Association of particles with J774 macrophages was monitored by flow cytometry.

Results: Through our novel polymeric platform we show that size, shape and mechanical stiffness can be controlled independently by the choice of template particle size, method of stretching, and hollow preparation of the particle, respectively. This highlights the versatility of our system to generate a gamut of polymeric carriers of controlled shape, size, and stiffness while retaining the same surface chemistry. Our results show that size and stiffness decrease the internalization for a spherical shape during phagocytosis. However, when the shape is altered to a rod the internalization is enhanced. These particles thus exhibit that shape and stiffness play a crucial role in the interactions of IgG functionalized particles with macrophages.

Figure 1a–c) 3µm Spheres , rods of varying stiffness d) Influence of size and stiffness on internalization.

Conclusions: Our polymeric system helps identify which combination of physicochemical parameters influence phagocytosis by macrophages and allows particle properties to be tuned to achieve desired particle-cell interactions. In addition, this particle platform can also be further extended to surface functionalization of active ligands or encapsulated molecules for modulation of macrophage activity and phenotype in immunological therapeutic applications.

References: