High Fc Density Particles Result in Binary Complement Activation but Tunable Macrophage Phagocytosis

TODD SULCHEK, PATRICIA PACHECO, Georgia Tech, DAVID WHITE, USDA — Macrophage phagocytosis and complement system activation represent two key components of the immune system and both can be activated through the presentation of multiple Fc domains of IgG antibodies. We have created functionalized micro- and nanoparticles with various densities of Fc domains to understand the modulation of the immune system for eventual use as a novel immunomodulation platform. Phagocytosis assays were carried out by adding functionalized particles to macrophage cells and quantitatively determined using fluorescent microscopy and flow cytometry. Complement system activation by the functionalized particles in human serum was quantified with an enzyme immunoassay. Our phagocytosis assay revealed a strong dependence on particle size and Fc density. For small particles, as the Fc density increased, the number of particles phagocytosed also increased. Large particles were phagocytosed at significantly lower levels and showed no dependency on Fc density. Complement was successfully activated at levels comparable to positive controls for small particles at high Fc densities. However at low Fc densities, there is a significant decrease in complement activation. This result suggests a binary response for complement system activation with a threshold density for successful activation. Therefore, varying the Fc density on micro/nanoparticles resulted in a tunable response in macrophage phagocytosis while a more binary response for complement activation.