Indian Institute of Science
Centre for BioSystems Science and Engineering
BSSE Annual Work Presentation

7th February 2020 (Friday), 4:00 PM, CES Seminar Hall, 3rd floor, Biological Sciences Building

Interactions of Nano- and Micro-Drug Delivery Systems With Phagocytic Immune Cells

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ABSTRACT

Macrophages are central players in host responses against biomaterials. Macrophages primarily function by either phagocytosing these biomaterials or encapsulating them as part of the frustrated phagocytosis process. A key goal to improve biomaterial compatibility is to reduce macrophage-material interactions, which may be achieved by altering the surface chemistry of the material. Among various surface modification strategies, polyethylene glycol (PEG) coatings are most commonly used. Previous work done by us (Sharma et. al. Biomat. Sci. 2019) showed that for sub-micrometer and micrometer-sized particulates, PEGylation slows the kinetics of macrophage interactions, but does not prevent uptake. If particulates of all surface functionalities are eventually taken up, then the question that comes up is, does this affect macrophage functionality? This question is especially important for materials that are slow degrading or non-degradable. Using very slowly degrading polystyrene (PS) particles as model systems, we demonstrate that macrophage functions are indeed altered following phagocytosis. Our studies focus on phagocytosis of fluorescently labeled PS particles of various sizes, by RAW 264.7 macrophages, primary human neutrophils or monocytes isolated from peripheral venous blood, and in C57BL6 mice. We observe that macrophages which have already phagocytosed one set of particles take up second set of particles in significantly higher numbers, as compared to cells that have not phagocytosed any particle. This effect is not caused by contaminating TLR ligands such as lipopolysaccharide. The uptake of particles does not cause any significant increase in ROS or NO production, indicating that the enhanced uptake is not due to activation of macrophages. These results from in vitro sequential uptake experiments correlated with both in vivo and ex vivo data. Experiments on bacterial neutralization capacity of immune cells suggests that their bactericidal ability may get altered post phagocytosis of particles. Comparison of transcriptome of macrophages with and without particles shows several genes that are differentially regulated, which may result in altered macrophage functionality. These results have potential implications in both the ability of the macrophage to respond against pathogens as well as initiate responses against biomaterials.