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Macromolecular Pairing On Nanoparticle Surface Modulates Immune Response

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Extended Abstract

Many nanoparticles in the blood activate the complement system, an integral part of the innate immune system that renders nanoparticles susceptible to phagocytosis by immune cells like polymorphonuclear leukocytes and tissue macrophages[1]. Complement activation by nanoparticles also compromises nanocarrier stability (e.g., liposome and lipid nanoparticles), causing drug leakage, promoting premature clearance of nanoparticles by the blood and tissue phagocytic cells, and compromising their therapeutic efficacy for intended non-phagocytic cell targets, and when uncontrolled, might induce adverse reactions and promote disease progression. Nanoparticle-mediated complement activation is multiparametric and is modulated by physicochemical properties including size, shape, and surface characteristics as well as non-specific protein binding [2], [3]. Recently, we showed poly (amido amine) dendrimers evade complement activation due to the Angstrom-scale spacing arrangement (the ASSA phenomenon) of their surface functional motifs [3]. Considering this, we hypothesise that immune cells might also respond differently to nanoparticles that display surface ligands/functional groups in ASSA arrangement. Here, we extend our studies by functionalizing polymeric nanoparticle surfaces with a library of fully characterised dendrimers and assess surface properties with a wide range of state-of-the-art biophysical modalities. The results show how precision surface patterning with dendrimers can control and modulate immune responses through assessment of serum protein deposition by shot-gun proteomics and macrophage challenge.

References

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