# Preventing Corona Effects: Multiphosphonic Acid Poly(ethylene glycol) Copolymers for Stable Stealth Iron Oxide Nanoparticles

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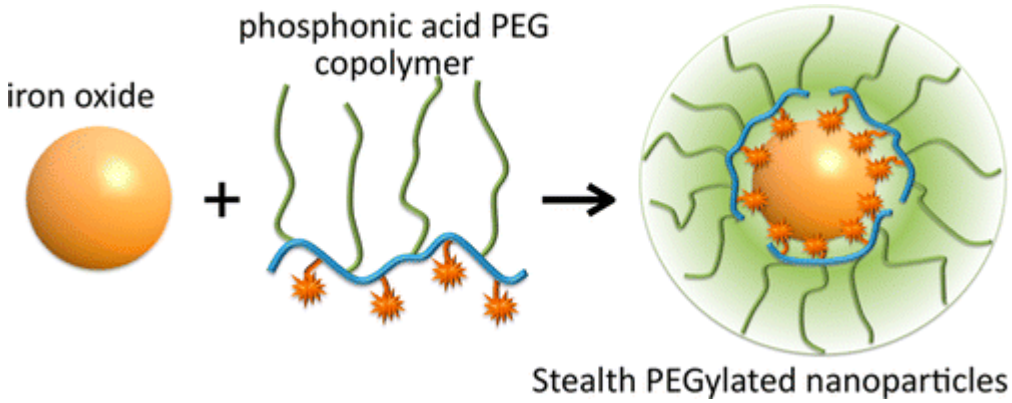
## Abstract




When dispersed in biological fluids, engineered nanoparticles are selectively coated with proteins, resulting in the formation of a protein corona. It is suggested that the protein corona is critical in regulating the conditions of entry into the cytoplasm of living cells. Recent reports describe this phenomenon as ubiquitous and independent of the nature of the particle. For nanomedicine applications, however, there is a need to design advanced and cost-effective coatings that are resistant to protein adsorption and that increase the biodistribution in vivo. In this study, phosphonic acid poly(ethylene glycol) copolymers were synthesized and used to coat iron oxide particles. The copolymer composition was optimized to provide simple and scalable protocols as well as long-term stability in culture media. It is shown that polymers with multiple phosphonic acid functionalities and PEG chains outperform other types of coating, including ligands, polyelectrolytes, and carboxylic acid functionalized PEG. PEGylated particles exhibit moreover exceptional low cellular uptake, of the order of 100 femtograms of iron per cell. The present approach demonstrates that the surface chemistry of engineered particles is a key parameter in the interactions with cells. It also opens up new avenues for the efficient functionalization of inorganic surfaces.