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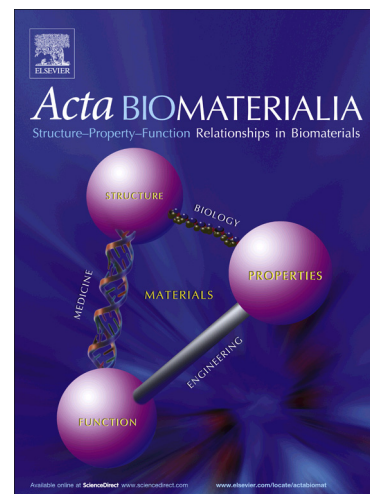
PEGylation of model drug carriers enhances phagocytosis by primary human neutrophils

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PEGylation of Model Drug Carriers Enhances Phagocytosis by Primary Human Neutrophils

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Abstract: Targeted drug carriers are attractive for the delivery of therapeutics directly to the site of a disease, reducing systemic side effects and enhancing the efficacy of therapeutic molecules. However, the use of particulate carriers for drug delivery comes with its own set of challenges and barriers. Among these, a great deal of research effort has focused on protecting carriers from clearance by phagocytes via altering carrier surface chemistry, mostly with the use of polyethylene glycol (PEG) chain coatings. However, few papers have explored the effects of PEGylation on uptake by freshly obtained primary human phagocytes in physiological conditions. In this work, we investigate the effect of PEGylation on particle uptake by primary human neutrophils *in vitro* and compare these effects to several cell lines and other model phagocytic cells systems. We find that human neutrophils in whole blood preferentially phagocytose PEGylated particles (e.g., ~40% particle positive neutrophils for PEGylated versus ~20% for carboxylated polystyrene microspheres) and that this effect is linked to factors present in human plasma. Model phagocytes internalized PEGylated particles less efficiently or equivalently to carboxylated particles in culture medium but preferentially phagocytosed PEGylated particles in the human plasma (e.g., ~86% versus ~63% PEGylated versus carboxylated particle positive cells, respectively). These findings have significant implications for the efficacy of PEGylation in designing long-circulating drug carriers, as well as the need for thorough characterization of drug carrier platforms in a wide array of *in vitro* and *in vivo* assays.

Keywords: Nanoparticles; Microparticles; PEGylation; opsonization; neutrophils; phagocytosis; particle drug carriers

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