**Nanotherapeutics: Towards Improving Safety and Efficacy**

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Nanotechnology has the potential to revolutionise clinical medicine for applications such as drug delivery and diagnostic imaging. Nanoparticles can be engineered to extend the circulation time of therapeutic drugs or stimulate beneficial immune responses (eg to vaccine antigens). However, despite the clear beneﬁts of such strategies, adverse responses can also be amplified. As increasing numbers of nano-based products come to market, safety concerns are also increasing.

Upon injection into the bloodstream, nanoparticles are immediately coated by serum proteins (the protein ‘corona’), commonly including albumin, immunoglobulins, complement proteins and coagulation proteins which play a critical role in determining the ensuing molecular and cellular responses to them. Within minutes, nanoparticles interact with platelets, leading to thrombin release and activation of the coagulation cascade. The complement system is also activated, promoting adverse hypersensitivity responses, rapid uptake of nanoparticles by phagocytic cells and clearance to lymphoid organs within minutes. These unwanted responses to nanoparticles can reduce therapeutic efficacy and hamper the translation of nanomaterials into the clinic.

This paper will discuss how the physicochemical properties of nanomaterials influence critical biological systems such as the coagulation and immune systems, and how these properties can be manipulated - either to limit deleterious responses (hypercoagulation, immune hypersensitivity responses or phagocytosis) and enhance circulation time, or to stimulate therapeutic immune responses (for immunotherapy and vaccine development). This information is essential to understanding the health impacts of nanomaterials and, ultimately, the development of safe effective nanotherapeutics.