Nanotools to understand why proteins and nanoparticles induce an immune response

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Abstract

Immunogenicity (i.e. the ability of a particular substance to provoke an immune response in humans or animals) represents a major challenge for the development of new biotherapeutics (Figure 1). It is essential to predict what induces such an immune response which sometimes may lead to autoimmune diseases. Nanotechnology plays an increasingly important role in predicting the immunogenicity. In the past few years, we have developed spectroscopic and imaging techniques to identify the features that make proteins of our bodies immunogenic. We have previously characterized the interaction of the blood protein platelet factor 4 (PF4) with heparin (anticoagulant) and other polyanions[1]. By circular dichroism spectroscopy we have found that an increase in antiparallel β-sheet content of PF4 above 30% is associated with binding of anti-PF4/heparin antibodies (or immunogenicity)[2]. We have also shown using isothermal titration calorimetry that ~11 monosaccharides are required to drive the structural changes in PF4 leading to immunogenicity [3]. Additionally, we have shown by single molecule force spectroscopy that at least three polyanion bonds have to be formed to each PF4 molecule to induce a conformation to which the antibodies bind [3]. In addition, by engineering hybrid micro/nano-arrays we have investigated the interaction of antibodies with complex antigens and have monitored the behavior of immune cells[4]. Our work has been extended to other blood or non-blood, soluble or transmembrane proteins possessing mutations or post-translational modifications.
Currently, we investigate immunogenicity of nanoparticles which are known to stimulate and/or to suppress the immune response by binding to blood proteins. Although the compatibility of the nanoparticles with the immune system is largely determined by their physico-chemical properties (*e.g.* size, shape, charge, surface groups), the effect of nanoparticle properties on the immune system is little explored. We study how nanoparticles may become immunogenic.

References

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Figures

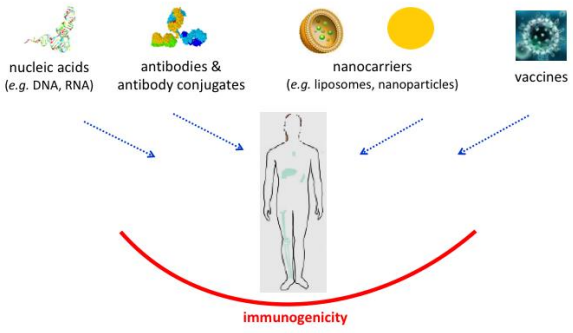

Figure 1: Schematic of nanobiotherapeutics which may induce immunogenicity.