Non-specific Adsorption of Complement Proteins Affects Complement Activation Pathways of Gold Nanomaterials

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The complement system is a key humoral component of innate immunity, serving as the first line of defense against intruders, including foreign synthetic nanomaterials. Although gold nanomaterials (AuNMs) are widely used in nanomedicine, their immunological response is not well understood. Using AuNMs of three shapes commonly used in biomedical applications: spherical gold nanoparticles, gold nanostars and gold nanorods, we demonstrated that AuNMs activated whole complement system, leading to the formation of SC5b-9 complex. All three complement pathways were simultaneously activated by all the AuNMs. Recognition molecules of the complement system interacted with all AuNMs in vitro, except for L-ficolin, but the correlation between these interactions and corresponding complement pathway activation was only observed in the classical and alternative pathways. We also observed the mediating role of complement activation in cellular uptake of all AuNMs by human U937 promonocytic cells, which expresses complement receptors. Taken together, our results highlighted the potential immunological challenges for clinical applications of AuNMs that were often overlooked.