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Protein Corona on Nanoparticles: Thermodynamics and Kinetics

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The food industry evolved from being just a source of nutrition, becoming a health and lifestyle promoter, using bioactive compounds and nanoparticles to enhance its products, creating functional foods. Nanoparticles (NP) are nanoscale materials ranging from 1 to 100 nm that possess unique physicochemical properties derived from their small size, large specific surface area and tunable surface characteristics. When introduced into environments with surrounding biomolecules, complexes are formed to lower their high surface free energy. The Protein Corona (PC) forms spontaneously on nanoparticle surfaces, this formation is a thermodynamic and kinetic equilibrium process of protein adsorption and desorption, resulting in a dynamic interfacial layer. This formation can be investigated by measuring changes in the properties of the underlying NPs, such as changes in their size, charge, density, mass, absorbance, and fluorescence. The biomolecular corona drastically redefines the biological identity and *in vivo* fate of nanoparticles, while protein adsorption enhances colloidal stability through electrostatic repulsion and steric hindrance. While the biomolecular corona enhances overall biocompatibility by creating a protective layer that mitigates cytotoxicity and membrane damage, this effect simultaneously masks surface-engineered ligands, reducing the nanoparticle's specific targeting capabilities. Studies show that NPs may have indirect toxic effects via conformational changes in adsorbed protein, denaturation and inducing fibrillations, and these changes may expose new antigenic epitopes or a loss of function. Therefore, understanding and controlling these interfacial nano-bio interactions is essential for the rational design of safe, stable, and targeted nanotherapeutics and delivery systems.

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