

One of the most promising strategies for fighting cancer is the drug delivery process using synthetic nanoparticles. Once in biological milieu, the nanoparticle surfaces get covered with a layer of biomolecules called the “Protein Corona”. The protein corona formation changes the nanoparticles interaction with the human body dictating a new fate for them. The protein corona composition is not only dependent on the nanoparticle itself, but also it is affected by the health condition of patients as recently discovered through the experimental studies. Here, the effect of disease on the protein corona formation is discussed through the molecular dynamics simulations. A multiscale simulation framework composed of Coarse Grained Molecular Dynamics (CGMD) and All Atom Molecular Dynamics (AAMD) was devised. Besides, the effect of disease on the protein nanoparticle interaction was modeled for the first time in MD simulations through introducing the main metabolite of each disease to the simulation box. During the CGMD stage, the umbrella sampling method was utilized to find the free energy profile of the protein approaching to the nanoparticle surface. The configuration with the minimum free energy was then backmapped to the all atom resolution to study the structural changes during the protein corona formation. The adsorption of the fibrinogen on the polystyrene surface was simulated for two different diseases of diabetes and hypercholesterolemia. The CGMD simulation results illustrate an increase in the protein corona formation free energy for both the disease. As a result, the amount of adsorbed protein increases. This finding is in line with an increase in the number of the contact residues obtained through the AAMD simulation. This accordance implies the significant role of the hydrophobic interactions in the amount of the adsorbed proteins. Also, the CGMD simulations hint at an increase in the adsorption enthalpy with introducing the metabolite of the diabetes to the simulation box. The increase in the enthalpy happens concomitant to an increase in the percentage of the aromatic residues in the contact residues. Thus, the π - π interaction is the main mechanism of the fibrinogen adsorption on the polystyrene. It is noticed from the simulation snapshots that some of the glucose molecules, main metabolite of diabetes, bridge protein residues to the nanoparticle so that the interaction is stronger leading to a higher adsorption enthalpy. For the hypercholesterolemia as there is not such an effect, the adsorption enthalpy decreases with increasing the metabolite concentration. Moreover, the simulation results demonstrate that the competition of different proteins for the adsorption on the nanoparticle surface is affected with introducing metabolites. It is concluded that diseases can have significant effect on the protein nanoparticle interaction. The current research paves the way to designing new strategies for engineering nanoparticles to be deployed in nano-medicine in accordance with specific health condition of each patient in the framework of personalized medicine.