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No Nanoparticle is an Island - the Dynamic Interaction between Nanoparticles and Plasma proteins

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What John Donne (1572-1631) said about men fits very well to a nanoparticle into the bloodstream. No nanoparticle is an island. In fact, it interacts in several ways with biomolecules and gets surrounded by the so-called corona. When it comes to drug delivery purposes, especially in chemotherapy, it is fundamental to know how this corona may affect the kinetics of a nanoparticle inside a body. Different studies show that it is important to take into account not only the size-dependent interactions of a nanoparticle with the tumor, but also the surface-dependent interactions with neighboring biomolecules. The whole thing goes well beyond the EPR effect [1].

Conceptually, the corona can be defined as a dynamic system involving the nanoparticle surface and biomolecules encountered in a biological fluid. Nowadays, its well accepted that the characterization of this nanoparticle corona is crucial to understand and predict the behavior of nanosystems inside the bloodstream and other physiological fluids [2].

Theoretically, all nanoparticles that are placed in contact with biological fluids will interact with biomolecules, in special with proteins dispersed in these media. The quantitative, as well as the qualitative pattern of proteins that will be adsorbed depends on several factors. For example, observing the huge variety of plasma proteins - thousands of them - it is logical to assume that different proteins will compete for adsorption sites on the nanoparticle surface. Therefore, the corona nature itself may vary for different nanoparticles and different biological fluids [3].

It is well accepted that the interaction between plasma proteins and the nanoparticles will respect first the concentration and secondly the affinity of the peptides for the nanostructure surface. Thus, the most abundant proteins tend to quickly adsorb to nanoparticles regardless of their affinity. This initial corona is then slowly enriched with proteins with higher affinity to the nanoparticle surface, until equilibrium is reached. This resultant dynamic corona will produce the real identity of nanoparticles, which will then face cells and tissues inside a biological system [2].

In a biological fluid where low affinity proteins are more concentrated, the events described above take place sequentially, initially producing a transient soft corona, with weakly adsorbed proteins, followed by the formation of a more rigid corona as the more nanoparticle-avid proteins are adsorbed. It is this hard, stabilized corona that will define the surface proprieties of a nanoparticle in a biological fluid [2,3].

Ever since the classical concepts of the enhanced permeation and retention (EPR) effect were described in the 1980's, nanotechnology emerged as an extremely attractive strategy to deliver chemotherapeutic drugs to tumor tissues [1,4]. The EPR effect is based on the fact that tumor tissues have aberrant, disrupted, permeable vessels with pores larger than 150 nm in diameter, while normal tissues have continuous vessels with smaller pores, varying from 2 to 100 nm in diameter. This pore size difference is used to deliver nanoparticles larger than 100 nm to the tumorinterstitium, improving the drug delivery to tumor tissues [5].

As mentioned in the previous paragraph, the EPR effect is basically supported by a size-dependent effect. Despite the strong evidence supporting the value of the EPR effect in chemotherapy, the current literature is also pointing towards the importance of the dynamic interaction between nanoparticles and corona proteins, as well as on how this complex will behave in a certain biological system [5].

Once formed, the protein corona may (1) increase the nanoparticle size and then affect its size-dependent properties, as described for the EPR effect; (2) target the delivery of a nanoparticle to a specific tissue; or (3) accelerate the recognition of the nanoparticle by immune cells. As an example, the deposition of some types of apoliproteins on nanoparticles surface can increase its permeability across the brain blood barrier. Also, the adsorption of opsonins on a nanoparticle reduces significantly the circulation time of nanoparticle due to the recognition by resident macrophages in the liver [6]. Understanding the nature of the corona formed on nanoparticles is thus useful for one to design a nanosystem intended for biological applications.

In general, hydrophobic and charged surfaces, especially cationic types, induce a quickly corona formation. The reasons for that are diverse, but can be explained by the usual negative charges of proteins, and by the strong immunogenicity of hydrophobic surfaces [3,7]. A classical strategy to increase the life-time of hydrophobic nanoparticles in the bloodstream is to cover the system surfaces with hydrophilic polymers, such as poly-ethylene glycol, which prevent the deposition of serum opsonins, delay the recognition by immune cells, and enhance the circulation time of the nano-carriers.

In conclusion, nowadays the characterization of the nano-based drug delivery systems is not restricted to the nanoscopic feature of these materials, but also has to take into count all the interactions these systems may establish with biomolecules. This functional characterization is useful for researchers to understand, modulate and design new drug delivery strategies using nanoparticles as drug vehicles.

References

1. Muehlmann L, Azevedo RB (2012) There is Plenty of Room at the Bottom for

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Improving Chemotherapy: Exploiting the EPR Effect with Nanotechnology. Chemotherapy 1: e116.

2. Lynch I, Dawson KA (2008) Protein-nanoparticle interactions. Nano today 3: 40-47.
3. Casals E, Pfaller T, Duschl A, Oostingh GJ, Puntes V (2010) Time evolution of the nanoparticle protein corona. ACS Nano 4: 3623-3632.
4. Matsumura Y, Maeda H (1986) A new concept for macromolecular therapeutics in cancer chemotherapy: mechanism of tumoritropic accumulation of proteins and the antitumor agent smancs. Cancer research 46: 6387-6392.
5. Schroeder A, Heller DA, Winslow MM, Dahlman JE, Pratt GW, et al. (2011) Treating metastatic cancer with nanotechnology. Nat Rev Cancer 12: 39-50.
6. Kreuter J, Shamenkov D, Petrov V, Ramge P, Cychutek K, et al. (2002) Apolipoprotein-mediated transport of nanoparticle-bound drugs across the blood-brain barrier. J Drug Target 10: 317-325.
7. Cedervall T, Lynch I, Lindman S, Berggård T, Thulin E, et al. (2007) Understanding the nanoparticle-protein corona using methods to quantify exchange rates and affinities of proteins for nanoparticles. Proc Natl Acad Sci U S A 104: 2050-2055.