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The Importance of the Protein Corona for Successful Nanodevice Design and Delivery

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Nanomaterials and nanodevices are increasingly employed as promising new tools in nanomedicine. Their appeal comes mostly from the fact that they could be small enough to directly interact with the cellular machinery and could also reach previously inaccessible targets, for instance the brain.

It is not unusual, though, to hear that while novel nanodevices designed for specific goals appeared infallible in vitro, they actually failed to show the same, or even a similar potency when probed *in vivo*, in their true final, context. This then elicits ordinary (and often comfortable) explanations evoking the complexity of living systems as compared to the lab tube. Considering the consistent amount of funding that is currently channelled to nanomedical/nanotherapeutic projects worldwide, as well as the predicted future increase in investment, it is imperative that the community make an effort to better elucidate the deep reasons for such failures, possibly on a molecular basis.

Among nanodevices, nanoparticles are practically used in many biomedical and nanomedicine applications [1,2]. When designed for drug delivery and imaging purposes, nanoparticle administration likely requires intravenous injections [3]. It has been established that upon contact with blood the particle surface is rapidly covered by selected blood plasma proteins, as well as other biomolecules, which form a so-called "protein corona" [4,5]. The composition of such corona appears not to be random, but rather it seems to be precisely determined by both the particle and protein physico-chemical features. Two different layers are found on the nanoparticle surface. An inner layer of selected proteins slowly exchanges, in a time frame of hours, with the environment and thus forms a hard corona, while weakly bound proteins rapidly exchange with free proteins, in significantly different time frames (subsecond to minute), thus forming the soft corona [6]. When nanoparticles move from a certain compartment in the body to another, a significant evolution of the corona occurs in the second biological solution, but the final corona still contains a "fingerprint" of its history. Therefore, what the designed target of the nanoparticle really sees *invivo* is the nanoparticle and its corona, which keeps a memory of its prior journey through the body. It could be postulated that the corona and its dynamic behavior may effectively hinder the property, i.e. the chemical features, for which the particle was designed, as aimed to specific targets, therefore constituting a substantial reason for many of the current nanobiotherapeutic failures. On the other hand, the corona could confer to the particle novel and advantageous properties, for example influencing its targeting.

The corona has been suggested to play a role in a variety of therapeutic-related issues, including nanoparticle toxicity. For example, graphene oxide nanosheets were shown to have considerably lower cytotoxicity when incubated with fetal bovine serum, thus allowing the corona to form [7]. In other cases a high particle toxicity still occurred in the presence of the corona [8]. In fact, the concept of protein/biomolecular corona is not restricted to nanoparticles, but it may apply to any nanodevice. The presence of increasing lines of evidence on the direct influence of the protein corona on cellular behaviors and targeting of nanoparticles and nanodevices should prompt the community to investigate the fundamental phenomena occurring when the nanoparticle, or the nanodevice in general, is put into its real biological context. Of course, this is not an easy goal to achieve in practice. The characterization of the dynamic processes leading to the formation of the corona can be achieved by a detailed physico-chemical description, which includes also the biochemical characterization of the structural and functional modifications occurring in proteins when present in the corona as compared to their normal conditions in solution. On the other hand, tools and approaches typical of cell biology and biomedicine are needed to practically assess the biological effect of the nanoparticle-protein corona. Some very recent attempts to study quantitatively the dynamics of the nanoparticle-protein corona, especially focusing on its time evolution [9,10] seem to be promising starting points to try to unravel the behaviour of the particle in complex biological fluids and compartments. The barrier is, nevertheless, conceptual. Scientists from different disciplines, from the basic life sciences to physics and clinical sciences, have to face the fact that any attempt aimed at increasing the potency of designed nanodevices will probably result in success only when arising from an active, cross-disciplinary cooperation. This may sound trivial and known, but it is fundamental that such an interdisciplinary dialogue is initiated in nanomedicine during its infancy in order not to waste time and money. The issue of how the protein corona can modify the fate of a nanodevice in human body is by itself a clear example of how, if nanoscience, chemistry, physics, and biology do not strongly interact with each other, no single nanomaterial will be of practical use in medicine.

References

1. Bhattacharyya S, Kudgus RA, Bhattacharya R, Mukherjee P (2011) Inorganic nanoparticles in cancer therapy. Pharm Res 28: 237-259.
2. Subbiah R, Veerapandian M, Yun KS (2010) Nanoparticles: functionalization and multifunctional applications in biomedical sciences. Curr Med Chem 17: 4559-4577.
3. Nemmar A, Hoet PH, Vanquickenborne B, Dinsdale D, Thomeer M, et.al. (2002) Passage of inhaled particles into the blood circulation in humans. Circulation 105: 411-414.

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4. Cedervall T, Lynch I, Foy M, Berggard T, Donnelly SC, et.al. (2007) Detailed identification of plasma proteins adsorbed on copolymer nanoparticles. Angew Chem Int Ed Engl 46: 5754-5756.

5. Mahmoudi M, Lynch I, Ejtehadi MR, Monopoli MP, Bombelli FB, et.al. (2011) Protein-nanoparticle interactions: opportunities and challenges. Chem Rev 111: 5610-5637.

6. Lundqvist M, Stigler J, Cedervall T, Berggard T, Flanagan MB, et.al. (2011) The Evolution of the Protein Corona around Nanoparticles: A Test Study. ACS Nano 5: 7503-7509.

7. Hu W, Peng C, Lv M, Li X, Zhang Y, et.al. (2011) Protein corona-mediated mitigation of cytotoxicity of graphene oxide. ACS Nano 5: 3693-3700

8. Choi J, Reipa V, Hitchins VM, Goering PL, Malinauskas RA (2011) Physicochemical characterization and in vitro hemolysis evaluation of silver nanoparticles. Toxicol Sci 123: 133-143

9. Casals E, Pfaller T, Duschl A, Oostingh G J, Puntes V (2010) Time evolution of the nanoparticle protein corona. ACS Nano 4: 3623-3632.

10. Dell'Orco D, Lundqvist M, Oslakovic C, Cedervall T, Linse S (2010) Modeling the time evolution of the nanoparticle-protein corona in a body fluid. PLoS One 5: e10949.