Personalized cancer-specific protein corona affects the therapeutic impact of nanoparticles

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Despite recent progress in nanomedicine, there is still a lack of efficient nanotherapeutics for cancer treatment.

When nanoparticles (NPs) are injected, they circulate the bloodstream and interact with biomolecules, creating a biomolecular shell. This shell of biomolecules surrounding the NPs consists mostly of proteins and is referred to as the Protein Corona (PC). The PC composition depends on various factors, including, but not limited to i) surface properties of NPs (e.g. surface chemistry and charge), and ii) experimental parameters (e.g. incubation time, pH, temperature). The impact of these factors on the formation of the PC has been widely investigated and is nowadays well known. However, the effects of the biological milieu (e.g. patient's health status, plasma vs serum) on the PC formation and composition have been underexamined and still need to be deeply clarified.

Recently, it has been demonstrated that the protein pattern constituting the PC of NPs exposed to plasma of cancer patients is different than that of the PC formed by exposure of NPs to healthy plasma. These variations can be miniscule but crucial in the fate of NPs. In fact, NPs surrounded by a PC lose their synthetic identity and acquire a new biological identity responsible for their biological destiny (cell targeting, accumulation, immune response).

In this work, we have studied the PCs formed around NPs using plasmas of patients with one of eight cancers to gain insights into the cancer-related variations of the PC composition and into their potential effects on the therapeutic efficacy of NPs. Our results confirmed that the same NPs incubated with plasmas of patients affected by different tumors have distinct PCs. Overall, this is the first wide study unveiling the specific PCs formed around NPs using plasmas of eight cancers. This comprehensive report acts as a tool for researchers in nanomedicine to design personalized nanotherapeutics in a cancer-specific manner for clinical applications.

Methods: Silica NPs were incubated with plasma of healthy subjects and cancer patients. NPs in the study were 100 nm in size and the PCs in each subject's plasma were characterized and compared using SDS-PAGE and LC-MS/MS. Plasmas of patients with one of 8 cancers have been employed: breast, rectum, lung, kidney, thyroid, uterine, bladder, ovary.

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