Detoxifying Antitumoral Drugs via Nanoconjugation: The Case of Gold Nanoparticles and Cisplatin

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Abstract

Last decade has seen a flourishment in the study of the properties of inogranic nanoparticles for medical applications. Nanoparticles display properties that are strongly determined by both morphology and environment and in the physico-chemical context where they are immersed, therefore allowing to monitor and manipulate biological states. In fact, inorganic nanoparticles behave as "artificial atoms", since their high density of electronic states -which controls many physical properties- can be extensively and easily tuned by adjusting composition, size and shape and used in biological environments. In fact, nanotechnology's ability to shape matter on the scale of molecules is opening the door to a new generation of diagnostics, imaging agents, and drugs for detecting and treating disease at its earliest stages. But perhaps more important, it is enabling researchers to combine a series of advances, creating thus nanosized particles that may contain drugs designed to kill tumours together with targeting compounds designed to home-in on malignancies, and imaging agents designed to light up even the earliest stage of cancers. In fact, a description of cancer in molecular terms seems increasingly likely to improve the ways in which human cancers are detected, classified, monitored, and (especially) treated, and for that, nanoparticles, which are small and therefore allows to address molecular structures in an unique manner, may be specially useful for those tasks.

Thus, Nanoparticles (NPs) have emerged as a potential tool to improve cancer treatment. Among the proposed uses in imaging and therapy, their use as a drug delivery scaffold has been extensively highlighted. However, there are still some controversial points which need a deeper understanding before clinical application can occur. Here the use of gold nanoparticles (AuNPs) to detoxify the antitumoral agent cisplatin, linked to a nanoparticle via a pH-sensitive coordination bond for endosomal release, is presented. The NP conjugate design has important effects on pharmacokinetics, conjugate evolution and biodistribution and results in an absence of observed toxicity. Besides, AuNPs present unique opportunities as drug delivery scaffolds due to their size and surface tunability. Here we show that cisplatin-induced toxicity is clearly reduced without affecting the therapeutic benefits in mice models. The NPs not only act as carriers, but also protect the drug from deactivation by plasma proteins until conjugates are internalized in cells and cisplatin is released. Additionally, the possibility to track the drug (Pt) and vehicle (Au) separately as a function of organ and time enables a better understanding of how nanocarriers are processed by the organism.