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The role of diagnostic molecular pathology in the era of targeted therapy

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In the era of targeted therapy, the assessment and evaluation of solid tumors in pathology is becoming more and more based on a combination of the histopathology and the molecular analysis of tumor tissues or liquid biopsy. In addition, the choice of treatment protocols is increasingly based on the molecular features of the tumor as a consequence of the rapid development of new cancer treatments that specifically target aberrant proteins present in tumor cells. Not only the number of patients eligible for targeted precision medicine, but also the number of molecular targets per patient and tumor type is rising. Therefore, diagnostic molecular pathology has attained much attention in the last few years. It is of utmost importance to determine the relevant molecular aberrations present in tumors for diagnostic, prognostic or predictive purposes. However, this is faced with several challenges. First, the molecular pathology lab has to meet the challenge of doing the required molecular tests using the limited amount of tumor tissues embedded in paraffin after formalin fixation in short turnaround time. Second, the choice of the detection method is critical, since the analytical methods should provide accurate, reliable and cost-effective results. Third, the validation of the test procedures and results is essential. In addition, participation and good performance in internal (IQA) and external quality assurance (EQA) schemes is mandatory. However, in spite of all these obstacles, molecular pathology is increasingly becoming an integral part of the diagnostic workup of most solid tumors, as well as, in determining prognosis and response to treatment. The list of molecular tests for breast, lung, colon, stomach, bone and soft tissue tumors are continuously increasing.

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The effect of surface functionalization upon the cellular uptake characteristics of upconversion nanocrystals

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Recently, the investigation of the interactions between nanomaterials and biological systems (known as nano-bio interactions) has spurred tremendous research interest in the field of nanotechnology. To improve the therapeutic potential of the nanoparticle (NP)-based vehicles for the intracellular delivery, it is crucial to systematically study the fate of NPs with uniformity of particle size, shape and surface charge, which are desired for elucidating the effects of these properties on cell uptake and bio-distribution. Anthanide-doped upconversion nanoparticles (UCNPs) provide a novel BBB delivery approach, as their shape/size/surfaces are tunable. Furthermore, these nanoparticles have excellent detection characteristics such as background free, photo stable, and deep tissue penetration. In this work, we compared a series of upconversion nanoparticles (UCNPs), including original UCNPs, OA-free UCNPs, DNA-modified UCNPs, SiO₂-coated UCNPs and PEG-conjugated UCNPs to analyze the principle factors that facilitate the transport of nanoparticles into the mouse NSC-34 motor neuron cells. It is found that UCNPs cellular uptake is mainly dependent on the dispersity in cell culture media. The surface charge plays an important role during this procedure as well. Specifically, PEG-conjugated UCNPs showed the most excellent cell uptake ability among these five types of UCNPs. While, the original UCNPs were primarily found attached on the cell membrane, because they formed aggregation in the cell culture media. The cytotoxicity of the UCNPs in NSC-34 cells demonstrated that the PEG-conjugated UCNPs possessed minimal cellular viability. Through this work, the results highlight the potential application of constructing a multifunctional UCNPs nano-composite with integration of brain drug delivery, diverse biomolecule monitoring and deep tissue imaging.

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