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Nanobiotechnology as a Versatile Toolkit for Developing Targeted Theranostics towards Cancer and Infectious Diseases

ABSTRACT:

Cancer and infectious diseases are poised to become the leading causes of human mortality in the twenty-first century. The key to effectively addressing these public health challenges lies in adopting theranostic approaches, which involve the integration of targeted, ultrasensitive diagnostics and therapy modalities to facilitate early diagnosis, enhanced therapeutic efficacy and improved patient outcomes. Nanoparticles possess higher chemical reactivity than particles of larger size due to their high surface-area-to-volume ratio, and are therefore, ideal platforms for integrating multiple targeting moieties, diagnostic, biosensing and therapeutic agents into multifunctional theranostic delivery vehicles. Hydrogel polymers are especially amenable to the development of multifunctional theranostic nanoplatforms for in vivo applications due to their biocompatibility and highly flexible physicochemical properties. We have demonstrated that multifunctional nanoplatforms, based on the synthetic hydrogel polymer, polyacrylamide, selectively deliver photoacoustic, MRI contrast, tumor delineation, chemotherapeutic and photodynamic agents to tumor cells (in vitro and in vivo), thus achieving highly efficacious cancer detection and cytotoxicity. The surface chemical engineering of the hydrogel nanoplatforms also plays a crucial role in increasing their circulating half-life in vivo, and mediating their selective internalization by the target cancer cells. More importantly, the surface chemical engineering of the nanoplatforms modulates the intracellular signaling pathways within the tumor cell following internalization, which in turn affects the subcellular site of delivery of the nanoplatforms, and chemotherapeutic efficacy.

Similarly, the early and rapid diagnosis of highly-pathogenic, slow-growing bacteria, such as Mycobacterium tuberculosis (M.tb; the causative agent of TB) is crucial to improving patient responses to TB therapy and restricting transmission of the pathogen. We exploited the Surface-Enhanced Raman Scattering (SERS) effect of silver nanoparticles (AgNPs) to enable rapid and sensitive SERS spectroscopic fingerprinting and discrimination of M.tb from other bacteria. This was achieved by in situ synthesis of AgNPs in the presence of the bacteria, such that the AgNPs formed within the bacterial cell walls, thereby permitting acquisition of SERS spectral signatures from the unique biomolecular constituents of the bacterial cell walls. The SERS spectral signature of M.tb is now being adapted to a rapid, low-cost, point-of-care diagnostic test to achieve quantitative detection of M.tb bacilli, without requiring expensive and laborious nucleic acid amplification or bacterial culture techniques.