Editorial: Nanomedicine for Treatment of Cancer

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Cancer is among the deadliest diseases faced by mankind, causing millions of deaths worldwide. [1] Decades of research into effective ways to fight cancer have provided therapeutic options such as chemotherapy, radiotherapy and curative surgery in order to control cancer progression and eradicate tumors. [2-5] However, due to the inherent complexity of cancer, it is still a tough task for scientists to truly cure this disease. Among available therapeutic alternatives, chemotherapy is considered the major approach in cancer therapy, as evidenced by the large quantity of prescriptions of chemotherapeutic drugs used in the clinic annually. While chemotherapeutic treatments provide benefits to many patients, the strong toxicity, poor tissue selectivity, narrow therapeutic windows and related drug resistance greatly limit the use of chemotherapeutic drugs and may adversely affect the quality of life of cancer patients. [6] In particular, the major cause of toxicity from chemotherapy is due to the off-target effects of the highly cytotoxic compounds used, which target physiological signaling pathways in non-tumor tissue and result in the death of healthy tissue. [7, 8]

The off-target effects of therapeutic agents led to the concept of the "magic bullet", a term developed by German Nobel laureate Paul Ehrlich over 100 years ago and which describes the selective delivery of an active drug specifically to diseased tissues but not normal and healthy tissues.[9] The precise delivery of drugs would allow the use of smaller doses of pharmaceutical and chemotherapeutic agents in a more targeted approach that eliminates the off-target effects of these drugs, thereby holding the promise to overcome and cure cancer.

Traditional pharmaceutical technology is limited in that it can only produce large, micrometer-sized delivery particles with limited capability for surface modification and targeting. Recent advances in nanotechnology have provided scientists with the ability to selectively generate nanoparticles of different sizes and properties for various objectives. Using top-down or bottom-up nanoparticle synthesis methods, scientists are now able to manipulate the size, shape, and internal and external physicochemical properties of nanoparticles. In addition, novel techniques are providing insight into mechanisms for drug loading onto these nanoparticles.[10, 11] Nanoparticles provide a huge promise for cancer therapy as nanoparticles show an enhanced permeability and retention (EPR) effect which permits these nanoparticles to specifically target tumor cells as well as accumulate in the tumor due to the leaky nature of tumor vasculature.

Both non-covalent encapsulation and covalent conjugation have been exploited to load active drugs into nanoparticles. In non-covalent encapsulation, drug molecules are loaded into nanoparticles by non-covalent bonding such as hydrogen bonding and π-π interaction. This offers the advantages of allowing the adjustment of the dosage ratio as well as the ability to deliver multiple drugs simultaneously as combination therapy, an approach that has been shown to improve the efficacy of cancer treatment.[12] However, the weak, non-covalent nature of the drug-nanoparticle linkage may lead to instability in the kinetics of drug release, leading to a rapid "burst" of drugs from nanoparticles and imprecise drug loading percentage. In comparison, covalent conjugates in which the drugs and nanoparticles are chemically bonded together enable the generation of a drug delivery vehicle having

a predictable drug release profile which can be adjusted by either the concentration of conjugates or the amount of attached drugs. [4, 13-15]

Therapeutic drug-nanoparticle conjugates are being developed and used in the clinic. One of the most successful examples of therapeutic nanoparticles is Abraxane® which uses albumin as a delivery vehicle for paclitaxel.[16] Paclitaxel is a drug from Taxane family that suppresses microtubule dynamics during cancer cell division. Abraxane® has an average nanoparticle size of about 130 nm and has been approved U.S. Food and Drug Administration (FDA) for the treatment of breast cancer, lung cancer and pancreatic cancer. While this is one example of nanoparticles in cancer therapy, there are currently more than 200 nanomedicines that are either approved for use or are in different stages of clinical trials.

The field of nanomedicine is still young. While great achievements have been accomplished in this field, there are still many essential questions for scientists to address regarding nanomedicine and its application in cancer therapy. These questions include the choice of biocompatible materials, the immunological response from delivery vehicles and the potential systemic toxicities of nanosized medicines.[17, 18] Answering these questions will allow the development of nanomedicine and will lead to enhanced targeting and treatment of cancer and other diseases.

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