Nanotechnology – A promising prospect for cancer diagnostics and therapeutics

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According to the World Health Organisation (WHO), 9.6 million deaths were reported from different cancers worldwide in 2018, making it the second most leading cause of death.[1] High mortality from various malignancies is attributed to the poor sensitivity and specificity of various diagnostic and therapeutic options available at present. Development of nanoparticles (NPs) has facilitated the targeted delivery of various medicines and diagnostic materials to specific tissues, resulting in increased sensitivity and specificity of existing diagnostic and therapeutic techniques as well as development of new novel approaches. Therefore, application of nanotechnology has shown tremendous potential in enhancing the diagnostic and therapeutic of various diseases including different types of cancers.[2]

NPs are defined as material with overall dimensions in the nanoscale (1-100nm). Particles on a nanoscale behave like nothing on large scales, as they have to satisfy the laws of quantum mechanics rather than semi-classical physics for microstructure/bulk materials. NPs have several unique properties in terms of their large surface to volume ratios giving them a very high chemical reactivity, quantisation of energy/quantum confinement allowing to be used as bioimaging agents and biological mobility, which are not present in macroscopic materials. NPs can be classified into different classes based on their properties, shapes and sizes. These include metallic NPs, polymeric NPs, lipid-based NPs and more recently polymer-lipid hybrid NPs.[2,3]

In targeted drug delivery, NPs protects the drugs from non-specific binding and allows for better tumour accumulation via passive and/or active targeting. Passive targeting is primarily driven by the enhanced permeability and retention (EPR) effect. Active targeting, on the other hand, relies on site-specific ligands (e.g. antibodies) used to functionated the surface of NPs. Alternatively, an on-site injection can be used for superficial tumours. Once at the tumour site, NPs can undergo cellular internalisation and intracellular drug release triggered by site-specific internal stimuli such as overexpressed proteolytic enzymes and acidic pH. NP formulations are being developed to deliver traditional chemotherapy drugs as well as non-toxic sensitising agents that only elicits a cytotoxic effect when they are activated by an external stimulus such as light, radiofrequency and low-intensity ultrasound.[2]

It has also offered the ability to develop non-invasive and effective theragnostic systems allowing for both diagnosis and treatment with a single agent such as photosensitive cyanine dyes.[4] Another form of nanotechnology-based cancer treatment being developed is localised magnetic hyperthermia using magnetic NPs and more recently thermo-chemotherapy, where traditional chemotherapy agents are combined with magnetic NPs in the same formulation. Ferrite NPs or iron oxide NPs are the most explored magnetic NPs up to date.

Once these particles are reduced to the nanoscale, they become superparamagnets, which means they only exhibit magnetic behaviour when an external magnetic field is applied. This, in theory, allows for magnetic targeting of the tumour site as an alternative to passive/active targeting but it has certain practical limitations such as possible damage to the blood vessels and surrounding tissues/organs. Once at the tumour site, these NPs can be made to vibrate by applying an alternating magnetic field. The heat is generated from the conversion of magnetic energy into heat energy.[2] We still need to better understand the in-vivo nanoparticle-tissue interactions. In particular, the formation of protein corona (a coating of proteins adsorbed from plasma and/or intracellular fluid) around the nanoparticles that not only changes their overall shape and size but also eliminates the functionality of any surface modalities.[5]

A retrospective study (2005-2015) of NP targeting efficacy revealed a median NP delivery of 0.7% to solid tumours.[6] Furthermore, there is a lack of research being carried out in nanotoxicity – toxic side-effects arising from particles on a nanoscale. Only an estimated 5% and 4% of EU's and US nanotechnology research budget is being spent on "nanotoxicity or impact on humans and the environment".[7] Generally, the

toxicity studies rarely go beyond the weight loss and the histology of organs. Since the idea is to improve therapies, side-effects need to be investigated thoroughly – even at preclinical stages. Nevertheless, if these issues are addressed properly, nanotechnology does offer a lot of potential for developing novel cancer diagnostic and therapeutic techniques with high tumour-targeting specificity and sensitivity.

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