



Nanoparticle delivers  
radiotherapeutic  
to a cancer cell.

Picture: Yaser Hadi Gholami

# Cancer nanomedicine: challenges and opportunities

Nanotechnology holds enormous promise for personalised cancer medicine — translation is the key

**M**edicine is on the cusp of a revolution. Personalised, precision medicine — designed and tailored at a molecular level for an individual's own physiological make-up — will become an inevitable reality in the 21st century. As with all paradigm shifts in medicine, this will be driven by new science and technology, and the technology of the 21st century is nanotechnology.

Nanomedicine is a rapidly evolving paradigm where nanoscience and nanotechnology are applied to medicine. The science underpinning nanotechnology is that some materials, when reduced from everyday, bulk scales down to nanoscales (billionths of a metre; smaller than the size of a typical virus), exhibit dramatically different physical properties. Harnessing and customising these unique nanoscale properties offer unique advantages to health and medicine for two reasons. First, many key molecules involved in biochemical processes responsible for regulating biological function have nanometre (nm) sizes (eg, a glucose molecule is about 1 nm), so nanoscale probes offer a means for molecular-based interrogation and intervention strategies. Second, because of their size, nanoprobings offer a relatively discreet, non-invasive strategy for disease detection and targeted therapy (although the immune system inevitably catches up).<sup>1</sup>

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An important example of how nanoscale properties can be harnessed for medical applications is magnetic resonance imaging. Here, image contrast is enhanced using magnetic nanoparticles, usually based on gadolinium or iron oxide, which exhibit strong magnetism only when reduced to scales of 20 nm or less.<sup>2</sup>

## Nanoparticles: size matters when it comes to targeting tumours

In cancer nanomedicine, a wide range of nanoparticles continue to be developed for better tumour-targeted delivery of therapeutics (chemotherapy and radiotherapy). These include liposome-, polymer- and micelle-based nanoparticles for encapsulated delivery, and metallic nanoparticles (eg, gold), which have been investigated for targeted radiotherapy.<sup>1-3</sup> There are two

types of tumour-targeting approaches with nanoparticles: passive and active. Passive targeting relies on tumour vasculature, which has larger endothelial gap junctions compared with healthy tissue. Nanoparticles greater than 8 nm can pass through these gaps to reach tumour cells. An enhanced permeability and retention effect results from the combination of larger gap junctions and defective lymphatic drainage, particularly around fast-growing tumours, facilitating preferential accumulation and prolonged retention in the tumour tissue.<sup>1</sup> In active targeting, however, nanoparticles are conjugated with targeting agents, such as antibodies, that are specific to proteins highly expressed by certain tumours (eg, human epidermal growth factor receptor 1 in non-small cell lung cancer).<sup>3</sup>

## Challenges: clinical translation

Despite ongoing progress in basic and preclinical cancer nanomedicine research, arguably the single most important challenge is clinical translation.<sup>4</sup> However, most of the many different nanoplatforms developed for cancer therapy have not progressed past Phase II clinical trials.<sup>1</sup> Very few have achieved United States Food and Drug Administration approval (eg, liposome-encapsulated doxorubicin and daunorubicin for breast and ovarian cancers, and Kaposi sarcoma). New efforts are focusing on the potential to extend the capabilities of other therapeutic and imaging nanoplatforms developed and approved for non-cancer indications. For example, ferumoxytol is an iron oxide nanoparticle used for treating anaemia and it is also a magnetic resonance imaging contrast-enhancing agent.<sup>5</sup> Nanotheranostics — the use of nanoplatforms combining targeted therapy and diagnostic imaging functionality — is a rapidly growing trend.

Why is bench-to bedside so challenging for cancer nanomedicine? The problems are many. Key difficulties include controlling nanoparticle size and preventing nanoparticle aggregation *in vivo*, which are critical for clearance by the kidney or liver. Biocompatibility, blood circulation time and the ability to elude the immune system long enough to release a therapeutic cargo, are similarly difficult to clinically validate. Additional practical challenges that need to be overcome for clinical translation include tumour cell specificity, cellular uptake and localisation, and controlled release and functionality of the cancer therapeutic.<sup>3</sup>

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## Opportunities: clinical translation

The challenges presented by clinical translation could equally be viewed as opportunities. This is the approach taken by the European Foundation for Clinical Nanomedicine (<https://www.clinam.org>). Similarly, the US National Cancer Institute (NCI) integrates translational and basic science research in its Alliance for Nanotechnology in Cancer (<http://nano.cancer.gov>). Launched in 2004, the Alliance held a strategic workshop in 2013, the outcomes of which highlighted several recommendations for future opportunities in cancer nanotechnology.<sup>6</sup> These include supporting the development of new techniques and clinical translation in parallel; supporting a stronger focus on developing

active targeting strategies; and giving a high priority to imaging probes and lower priority to developing in-vitro nano-enabled techniques. The NCI report also highlighted the importance of interdisciplinary collaboration — bringing together clinical and basic science researchers from diverse backgrounds is the key to creating unique opportunities for genuine breakthrough discoveries in cancer nanomedicine.

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