

Can nanotechnology help push the limit for early cancer diagnostics?

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Opinion

Cancer is a leading cause of death across the globe. The menace of this deadly disease calls for an urgent need to develop new treatment methods in the form of advanced cancer therapy. This involves early-stage imaging, delivery and precise targeting of pharmaceutical, therapeutic and diagnostic agents for cancer prevention, better diagnosis, imaging, and eventually killing the diseased cells. Early screening of cancer is very important for proper diagnosis and therapy. Current diagnostic tools/imaging techniques such as X-rays, computed tomography, ultrasound, radionuclide imaging and Magnetic Resonance Imaging (MRI) as well as tissue biopsy and bioanalytical assay of body fluids by enzyme linked immunosorbent assay (ELISA) have been used for cancer screening and staging, determining the efficacy of cancer therapy and monitoring recurrence. Unfortunately, most tumors are detectable only when they reach a certain size and contain millions of cells that may have already metastasized (transfer of disease from one organ or part of the body to another not directly connected with it). Therefore, applications of these techniques are limited due to the lack of sufficient sensitivity to detect small numbers of malignant cells in the primary or even metastatic sites.¹ It is also difficult to detect specific cancer cell-surface markers, which are not only a target for cancer therapy but can also assist in the diagnosis and staging of cancer. Other challenges include inadequate drug concentrations reaching the tumor and the limited ability to monitor therapeutic responses thus leading to significant complications such as multidrug resistance due to poor drug delivery.¹

Recent advances in nanotechnology have immensely contributed to the development of multifunctional nanoparticles that can target a tumor or tumor-specific delivery of imaging probes, deliver therapeutic drugs or genes, respond to external triggers to release the agent and also monitor the therapeutic response.¹⁻⁵

Multifunctional nanoparticles can be fabricated from different materials in a variety of compositions. These include quantum dots, polymeric nanoparticles, gold nanoparticles and superparamagnetic nanoparticles.² This multifunctionality is generated by combining these nanoparticles with a specific targeting agent for imaging, a cell penetrating agent for drug release and any suitable stabilizing polymer to generate biocompatibility etc. These nanoparticles provide several unique features and capabilities in comparison with conventional in-vivo imaging probes or contrast agents. Firstly, being 100- to 10,000- fold smaller than cancer cells, these can easily transfer or penetrate through blood vessels and interact with targeted tumor-specific proteins. Secondly, their optical and electronic properties can be tuned by simply varying their size. These size-dependent tunable properties can be used for simultaneous detection of multiple cancer biomarkers. Thirdly, their high surface area can be leveraged towards attachments of a variety of functional groups that can be linked to different diagnostics and therapeutic agents. In addition, recent research has also shown that smaller nanoparticles (1-100 nm) tend to preferentially accumulate at the tumor sites which eventually

results in the leakage of accumulated circulating nanoparticles into the tumor sites or tissues. This enhanced accumulation of nanoparticles can mainly be attributed to the poor lymphatic drainage of growing tumors (a condition of localized fluid retention and tissue swelling caused by a compromised lymphatic system). These novel features of nanoparticles offer exciting possibilities to develop new treatment methods for advanced cancer therapy that would allow customized and targeted drug or imaging agent delivery and subsequent destroying of cancer cells.¹⁻⁵

It is essential that nanoparticles remain in the bloodstream for a reasonable period of time in order to reach the targeted tumor tissue. During circulation, they are caught in the spaces between the cells in the tissues (extracellular matrix proteins). To overcome this problem, one viable approach is to coat nanoparticles with hydrophilic polymers. Hydrophilic coating can efficiently increase hydration along with protecting nanoparticles from capture by matrix proteins. This helps enhancing biocompatibility of nanoparticles.³ Multifunctional magnetic nanoparticles have been synthesized for simultaneous cancer cell-specific delivery of hydrophobic anticancer drugs, magnetic resonance and fluorescence imaging, magnetic manipulation and cell targeting. To demonstrate the potential of the synthesized nanoparticles for cancer therapy, water-insoluble anticancer drugs were delivered into human cancer cells. The targeting ligand modification increased the drug payload delivery into human cancer cells relative to that into non-cancerous cells. The approach allows nanoparticles to be monitored inside living cells both by magnetic resonance and fluorescence imaging methods. This can be simultaneously used as a drug delivery vehicle.⁴

Currently, inorganic nanomaterials including gold nanoparticles and super paramagnetic iron oxide nanoparticles (SPION) have been reconnoitered as potential contrast agents for cancer imaging. In more advanced development in cancer imaging, nanotechnology promises to improvise the current existing imaging platforms such as endoscopic ultrasonography (EUS) or MRI cholangiopancreatography (MRCP) for pancreatic cancer imaging of pancreatic cancer.^{6,7}

Nanotechnology also offers tremendous opportunities in diagnosis of cervical cancer compared to commonly used techniques of cytology and HPV detection, which are challenged due to the lack of sensitivity, especially in detecting pre-invasive cervical cancers. The detection of HPV genes could help diagnose cervical cancer at a very early stage and thus enhance cancer treatment efficacy.⁸

Conclusion

In conclusion, we foresee significant breakthroughs happening in the future in multifunctional nanoparticle based cancer therapy. Nanoparticle-based targeted delivery systems could revolutionize the diagnosis and treatment of cancer in the future. There are plenty of opportunities for interdisciplinary collaborations between physicists, chemists, engineers, biologists and clinicians to address research questions at the level of fundamental biology and science to develop novel nanoparticles and systems, particularly enabling cost-effective and large-scale production of multifunctional nanoparticle drug delivery systems for the diagnosis and treatment of cancer. However, for transition from laboratory to clinical practice, we need to overcome and address the toxicity issues of nanoparticles.

Acknowledgments

None.

Conflicts of interest

None.

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