Spare the rod

Nanomaterials expert **Dr Xiaohua Huang** explains her particularly ambitious project to combat cancer with structured nanoparticles such as gold nanorods and iron oxide-gold hybrid nanoparticles

DR XIAOHUA HUANG

Can you describe how you became interested in the development of novel inorganic nanomaterials?

This subject caught my attention when I was a PhD student at Georgia Institute of Technology. Georgia Tech is a hub of nanotechnology and I was fascinated by the research taking place in this field there. My research advisor Professor Mostafa A El-Sayed had been investigating fundamental properties of gold nanoparticles for years before I joined his group. I worked with him to open a new research direction towards developing gold nanoparticles, especially gold nanorods, for light scattering cancer imaging and photothermal therapy. During my continued postdoctoral training at Emory University, USA, working in Professor Shuming Nie's lab, I became interested in magnetic nanoparticles and was impressed by the power of this kind of material in cancer detection and treatment. These wonderful research experiences in such prestigious groups have motivated my continued efforts in the field of cancer nanomedicine, as exemplified by my independent research at the University of Memphis, USA.

What motivates and fascinates you most about this area of research?

Cancer remains the leading cause of death in the US, killing about half a million people each year. Nanotechnology has proven promising for developing new diagnostic and therapeutic products because nanoscale materials have exceptional properties that are not available to individual molecules or bulk materials. The goal of my research is to develop nanotechnology-

The gold standard

Treating cancer is all about catching it early. A team of researchers at the University of Memphis, USA, is developing a novel method for detecting and characterising disease with a minimally invasive liquid biopsy

CANCER IS MOST people's nightmare diagnosis, but the truth is that 90 per cent of the time, it is not the original tumour but its metastases that are lethal. Some types of cancerous cell are able to circulate freely in the bloodstream, and it is these circulating tumour cells that are responsible for settling and proliferating in new parts of the body, causing metastasis. As well as posing a significant hazard, however, circulating tumour cells also present cancer researchers and health professionals with an opportunity: they can be used as biomarkers. Present in blood, they offer the potential to detect cancer and metastases at an early stage, determine prognosis and personalise therapy through a non-invasive liquid biopsy.

Circulating tumour cells are such a powerful indicator of disease progression, in fact, that they have already been used to identify cancer before the tumours themselves have even been spotted with imaging techniques. So why are these telltale cells not being exploited in clinics? There are two reasons for this. Firstly, they are very hard to find; 1 ml of blood, one might find 5 billion red blood cells, 10 million white blood cells, and only one or two circulating tumour cells. The second reason is that these cells, similar to the cancers they come from, are highly heterogeneous and can have a wide variety of identifiable molecular characteristics. In short, finding circulating tumour cells in a patient is like searching for a needle in a haystack when you are not certain what a needle looks like.

NIFTY NANOPARTICLES

Fortunately, there is a group at the University of Memphis in the US that is endeavouring to make this process much easier. Dr Xiaohua Huang leads a laboratory within the institution's Department of Chemistry that makes use of a number of approaches in order to accomplish this goal – including advanced analytical microscopy, versatile microfluidic devices and, most importantly, multifunctional nanomaterials. The nanoparticles that the Memphis scientists work with range from gold nanorods to iron oxide-gold core-shell nanoparticles, and can fulfill functions from the destruction of cancer cells to the transport of drug molecules – as well as being ideal for detecting circulating tumour cells.

The method devised by Huang and her collaborators relies on hybrid iron oxide-gold core-shell nanoparticles – tiny particles that enjoy both the magnetic properties of the iron oxide core and the optical properties of the gold shell. These nanoparticles are then based tools to help cancer detection and treatment, and ultimately improve cancer patient survival.

How have your research interests evolved since you completed your PhD in 2006?

As a PhD student in 2006 in El-Sayed's lab, my research focused on the development of gold nanoparticles for cancer imaging and photothermal therapy. At Emory University, working with Nie, I investigated *in vivo* tumour targeting and uptake using gold nanorods as the model nanomaterials. After I joined the University of Memphis in 2010 as a tenure-track faculty, my research moved in three major directions: synthesis and understanding of the properties of novel magnetic-plasmonic core-shell nanoparticles; development of a novel integrated technology platform for capturing, detecting and molecular profiling of circulating tumour cells in blood; and development of novel combination cancer treatments to improve cancer therapeutic efficacy.

To what extent does your interdisciplinary research have a broad translational potential – not only for health but in other applications?

The technologies and products that we develop can be translated into early cancer detection and personalised cancer treatment, but they can also be used in other areas such as food science to detect pathogens.

Can you summarise your research on anisotropic magnetic-plasmonic core-shell nanoparticles and highlight its potential impact in the health field?

Due to their high integrity, facile surface chemistry, excellent stability, dual functions from the shell and core, and the intrinsic shape-dependent optical properties of their metallic shells, anisotropic magnetic-plasmonic core-shell nanoparticles are very promising in a wide range of applications across science, engineering and biomedicine. We have developed a method to make magnetic-plasmonic iron oxide-gold core-shell nanoparticles in several shapes including oval, pin and star. These nanoparticles show surface-enhanced Raman scattering activities between 30 and 40 times stronger than those seen in conventional spherical iron oxide-gold core-shell nanoparticles. Thus, these nanoparticles have great potential for developing highly sensitive analytical assays for cancer detection.

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linked with cancer-targeting antibodies and coated with tags that make them visible to Raman spectroscopy. The resulting product is ideal for capturing circulating tumour cells in whole blood; it binds with these cells and then a magnet placed under the flow vessel can capture the now-magnetic aggressor. The gold coating of the nanoparticles ensures that they give a good signal to the Raman spectroscope, allowing the trapped tumour cells to be identified and characterised.

EXPERIMENTAL CONFIRMATION

In a paper published earlier this year, Huang's team demonstrated the efficacy of their innovative method using breast cancer cells in whole blood. The experimental setup involved passing the spiked blood through a microchannel using a syringe as a pump. The channel was placed over a pair of magnets and the Raman spectroscope collected data from the captured and concentrated cancer cells.

The results of this experiment demonstrated that this method is indeed a sensitive and promising way of capturing and detecting cancer cells in whole blood – the detection limit was set at one or two tumour cells per ml of blood.

Huang is hopeful that this tool will provide the basis for the next generation of circulating tumour cell isolation, detection, enumeration and molecular characterisation. "By making use of the high sensitivity and specificity surface-enhanced Raman scattering technology and the powerful iron oxide-gold core-shell nanoparticles, we expect to generate a simple yet enabling technology platform," she explains. Of course, before this platform can be used in the clinic, the technology will need to be validated with further experiments and compared with current clinical solutions – but these challenges aside, the work of Huang and her colleagues may soon secure a golden future for cancer patients everywhere.

INTELLIGENCE

CAPTURE AND DETECTION OF CANCER CELLS IN WHOLE BLOOD WITH MAGNETIC–OPTICAL NANO-OVALS

OBJECTIVES

To develop new diagnostic and therapeutic tools for cancer using nanotechnology. Of particular interest are colloidal metal nanoparticles such as gold nanorods and dual functional nanoparticles such as iron oxide-gold hybrid nanoparticles for cancer detection and treatment, including magnetic separation and surface-enhanced Raman scattering detection of circulating tumour cells, light-activated combination cancer therapy and targeted *in vivo* drug delivery.

KEY COLLABORATORS

Professor Yongmei Wang; **Professor Sanjay Mishra**; **Professor Bashir Morshed**, University of Memphis, USA

Dr Daruka Mahadevan, University of Tennessee Health Science Center and The West Clinic, USA

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CONTACT

Dr Xiaohua Huang
Assistant Professor

Huang's Nanomedicine Group
Department of Chemistry
University of Memphis
Memphis
Tennessee 38152
USA

T +1 901 678 1728
E xhuang4@memphis.edu

http://bit.ly/Huang_lab

XIAOHUA HUANG received her PhD in Chemistry at Georgia Institute of Technology in 2006. After postdoctoral training at the Institute and Emory University, she joined the University of Memphis as a tenure-track faculty in 2010. In addition to her research activities in cancer nanomedicine, Huang teaches both undergraduate and graduate students at the University and supervises the research of PhD students. She has published over 30 peer-reviewed journal articles with more than 6,000 citations. Huang is regularly invited to speak at both national and international events and conferences. Her work has been recognised by the American Association for Cancer Research – Women in Cancer Research Brigid G Leventhal Scholar, Oak Ridge Associated Universities' Ralph E Powe Junior Faculty Enhancement Award and Early Career and Research Award in College of Arts and Sciences at the University of Memphis.

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