Using irradiated gold nanoparticles to treat cancer

Dr Victoria Timchenko
E: v.timchenko@unsw.edu.au
W: www.research.unsw.edu.au/associate-professor-victoria-timchenko

Research Objectives
Dr Victoria Timchenko researches the use of irradiated gold nanoparticles to treat cancer.

Detail
Address
2/26 Mount St Coogee,
New South Wales 2034,
Australia

Bio
Dr Victoria Timchenko is an associate professor at the School of Mechanical and Manufacturing Engineering, University of New South Wales, Sydney. She completed her PhD in engineering at the Institute for Problems in Machinery, Ukrainian Academy of Sciences, Kharkiv. Her areas of expertise are computational fluid dynamics and heat transfer. Research interests include natural convection and phase change problems; cooling of building-integrated photovoltaic systems and microelectronic devices; modeling of nanoparticles in human arteries; and nanoparticle hyperthermia for biomedical applications.

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Collaborators
- Leonid A Dombrovsky
- Michael Jackson
- Xi Gu
- Guan H Yeoh
- Robert A Taylor
- Darson D Li
- Stella M Valenzuela
- Bruce A Cornel
- Amani Alghalayini

References

Personal Response
What are your future research plans for investigating treatments using antibody-conjugated nanoparticles?

My future research plans involve development and synthesis of magneto-plasmonic nanoparticles optimised for hyperthermia and medical imaging. This includes but is not limited to:

a) the development of a computational and experimental methodology for the prediction of nanoparticle (NP) agglomeration under the influence of a range of passive and active external stimuli, such as pH and external magnetic field, and investigation of the role of plasmonic and magneto-plasmonic NP aggregation on the optical absorption and scattering properties

b) in vitro cell experiments to develop modified NPs that are capable of controlled selective aggregation and disaggregation when located within biological environments.
Using irradiated gold nanoparticles to treat cancer

Thermal therapy or hyperthermia uses heat to target infected tissue and cancer cells that resist radiotherapy. Despite promising clinical results, there remain difficulties with the approach, such as controlling heat generation and temperature distribution in diseased tissues and protecting surrounding healthy tissues from overheating. To improve the precision of the hyperthermia technique, Dr Victoria Timchenko from the University of New South Wales in Sydney, Australia, is developing a new technology using gold nanoparticles (GNPs) to treat radiotherapy-resistant cancers.

Laser-induced hyperthermia has been developed as a technique for cancer treatment, which involves heating tumour tissue via a laser beam directed through minimally invasive fibre optics. In some instances, it can be used in combination with radiotherapy and chemotherapy. Tissues are typically heated to a temperature within the range of 39–45°C which affects tumour tissues that have lower heat tolerance than normal cells. There are drawbacks to this technique: controlling heat generation and temperature distribution in diseased tissues is difficult and it’s hard to not overheat healthy tissue nearby.

To address these issues, Dr Victoria Timchenko from the University of New South Wales in Sydney, Australia, has been investigating an emerging new treatment for improving heating efficiency in hyperthermia applications: gold nanoparticles (GNPs).

**GOLD NANOPARTICLES FOR CANCER TREATMENT**

Hyperthermia treatment is delivered through minute probes that emit a laser beam of a specific wavelength, usually over a localised area, although whole-body procedures are sometimes carried out. The optimal wavelength for heat treatment is 700–900 nm, which falls within the near-infrared (NIR) region of the electromagnetic spectrum. While temperatures of 42 to 50°C cause significant cell damage, killing most of the irradiated cancer cells, Timchenko has optimised a new method that can selectively target tumour cells, raising the local temperature within a tumour to 60°C while leaving healthy tissue untargeted. The technique involves a phenomenon known as plasmonic resonance, the emission of heat that occurs when the free electrons of a metal are hit with light at very specific wavelengths.

Timchenko tested the phenomenon of plasmonic resonance of gold nanoparticles (GNPs) and found that when the GNPs are irradiated with NIR light, the localised heat generation could be significantly enhanced, offering promising results for the treatment of cancer. The nanoparticles can be chemically linked to specific antibodies that can penetrate blood vessels and selectively target cancerous cells. Once they have reached their destination, the GNPs can then be irradiated by the NIR light from non-invasive laser probes, which causes irreversible damage to all or most of the cancer cells treated. The correct insertion of the probes can be monitored using imaging techniques, such as CT scans. The simulation was used to predict and quantify the amount of light absorbed by cells in relation to increasing amounts of particles that make up the GNP clusters.

**BEHAVIOUR OF GOLD NANORODS**

Timchenko and her team have also published findings on the behaviour of gold nanorods (GNRs) and different concentrations of GNR solutions under near-infrared irradiation. Their 2018 study is of particular significance for hyperthermia applications, given that previous research reported that the heat-generating efficiency of gold nanorods is much higher than that of nanospheres and nanoshells. Most of the particles were single nanorods, although some assemblies were also present. The GNRs in the samples preferentially formed numerous side-by-side assemblies, although some end-to-end assemblies were also formed. As in the other studies discussed above, the team’s investigation of GNRs and GNP solutions was carried out both numerically and experimentally.

The researchers compared experimental data to a numerical simulation of the heat transfer between GNPs and the cell membrane. The interface comprises a gold film substrate attached to a lipid membrane architecture known as tethered lipid membrane (tBLM). The tBLMs are attached to an electrode enabling direct measurements of the membrane conductance which can be correlated to heat generated.

The spectra of end-to-end and side-by-side GNR assemblies were also investigated in the study, showing that when the rods clustered end-to-end and less than 10nm apart there was a peak in the absorbance of infrared light at the wavelength of 1100nm. Since the heat generated from the nanoparticles depends on the light absorbed, and human skin tissues only weakly absorb light with wavelengths between 700 and 900nm, the researchers concluded that it may be possible to preferentially, and beneficially, control particle clustering to accurately gauge the heat generation of GNR hyperthermia treatments.

A PROMISING NEW APPROACH

Since 2009 Timchenko has initiated a number of international collaborations to investigate and model the potential of GNRs and GNPs for cancer treatment, work which has already contributed to improvements in the thermal treatment of tumours. As the temperature reached during the treatment can be increased significantly when gold nanoparticles are irradiated with near-infrared light, Timchenko and her team optimised the conditions at which the nanoparticles are most effective, investigating both numerically and experimentally how the heat generation depends on the shape and the mode of aggregation of the nanoparticles. The results of the 2022 study will enable medical practitioners to finely control particle aggregation by adjusting the pH levels of the medium. This new understanding promises to significantly improve treatments for radiotherapy-resistant cancer tumours.
Partnership enquiries: simon@researchfeatures.com

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Partnership enquiries: simon@researchfeatures.com