NEW THERAPEUTICS

Heating things up

Thermal ablation therapy is being developed as a less invasive alternative to surgery to remove solid tumours. This approach, which can involve the use of lasers, microwaves or ultrasound to deliver a lethal dose of heat to the tumour, is limited by low penetrance and non-specific effects. Jennifer West and colleagues show that metal nanoshells, which produce heat when exposed to near-infrared (NIR) light, are a more effective way to achieve photothermal destruction of tumours.

Nanoshells are 100 nm particles that consist of a spherical dielectric core surrounded by a thin metal shell. Light induces collective oscillations of conductive metal electrons at the nanoshell surface, resulting in the production of heat. The authors fabricated nanoshells with a core of silica surrounded by a thin shell of gold. These particles are unique in their ability to become activated by NIR light (820 nm) — a wavelength that is able to penetrate tissue without being absorbed by it.

Previous studies have shown that NIR light can penetrate tissue at depths of more than 1 cm with no observable damage, and the authors showed that human breast cancer cells that were irradiated with NIR light from a low-power diode laser remained viable. Cells that were first incubated with the nanoshells and then exposed to NIR light, however, underwent a loss of membrane permeability and died.

But what happens *in vivo*? Nanoshells were injected interstitially into transmissible venereal tumours that were grown in the hind legs of mice. Despite the local injection of nanoshells only 5 mm into the tumour, they were found to diffuse throughout the tumour volume. Following exposure to NIR light, these tumours underwent an average temperature increase of 38°C at a depth of 2.5 mm beneath the dermal surface. The treatment, which was monitored using real-time magnetic resonance temperature imaging, was found to cause irreversible thermal damage that was confined to the tumour space. Histological analysis revealed coagulation, cell shrinkage and loss of nuclear staining in NIR-exposed regions. By contrast, the temperature in nanoshell-free tumours increased by only 9°C following exposure to NIR light — a temperature that did not cause irreversible tissue damage.

Now that a combination of nanoshells and light wavelength has been discovered that is safe and effective for therapy, this approach can be tested further to monitor the effects on survival and overall tumour regression. Because the gold surface of the particles can also be conjugated to antibodies and other molecules, it might be possible to systemically inject the nanoshells and achieve tumour-specific targeting.

Kristine Novak

References and links

ORIGINAL RESEARCH PAPER Hirsch, L. R. *et al.* Nanoshell-mediated near-infrared thermal therapy of tumors under magnetic resonance guidance. *Proc. Natl Acad. Sci. USA* **100**, 13549–13554 (2003)

WEB SITE

Jennifer West's lab:
http://bioe.rice.edu/FacultyDetail.cfm?RiceID=495