gliding and the structural chassis of the protozoa' commented Jean-Francois Dubremetz (University of Montpellier, France; http://www.univ-montp2.fr).

In conclusion, Joseph Schwartzman from the Dartmouth-Hitchcock Medical Center, NH, USA (http://www.hitchcock.org/) told *Drug Discovery Today* that 'This work opens up the possibility of finding a way to pharmacologically interfere with an essential function in the parasite's life cycle'. He continued, 'Motility is a novel drug target, but the unique mechanism of the glideosome makes it likely that it can be disrupted selectively from host cell functions'.

References

1 Gaskins, E. *et al*. (2004) Identification of the membrane receptor of class XIV myosin in *Toxoplasma gondii*. *J. Cell Biol*. 165, 383–393
2 Wells, W. (2004) An anchor for motoring. *J. Cell Biol*. 165, 294
3 Opitz C, and Soldati D. (2002) 'The glideosome': a dynamic complex powering gliding motion and host cell invasion by *Toxoplasma gondii*. *Mol. Microbiol*. 45, 597–604

New ray of hope for cancer patients

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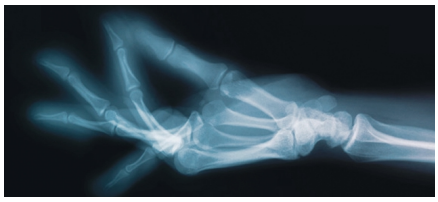
By using radiation-induced gene therapy to increase the amount of nitric oxide in tumour cells, researchers at the University of Ulster (http://www.ulst.ac.uk) have doubled the efficacy of radiotherapy in mice [1]. Their research has been seminal to a lot of work that other gene therapy groups are now doing with the radiation-inducible WAF1 promoter.

Nitric oxide synthase

Nitric oxide, a signaling molecule with important regulatory functions in most tissues of the body, has enormous potential as an anticancer agent because of its cytotoxic effect at higher doses. In addition, nitric oxide sensitizes cells to the effects of radiation and chemotherapy. Various research groups are therefore working on gene-therapy approaches to deliver the inducible nitric oxide synthase (iNOS, the enzyme responsible for generating nitric oxide in the body) to tumour cells. However, many of these approaches suffer from a lack of specificity for the target cells.

In the *Journal of Gene Medicine*, David Hirst and colleagues recently reported a strategy to overcome this problem. 'What they come up with here is a neat trick, because they have used the promoter to WAF1 or p21, which we know is […] a radiosensitive promoter,' says Lawrence Young, who develops novel gene therapy approaches for the



treatment of cancer at the University of Birmingham (http://www.bham.ac.uk). The promoter can be switched on by an external X-ray beam at radiation doses within the therapeutic range (2–4 Gy); the X-ray beam is targeted to cancer cells, thus limiting nitric oxide production to these cells. Then, the investigators can come in with higher-level doses of radiation (10–20 Gy), and that, combined with the cytotoxic effects of nitric oxide, results in a significant antitumour effect.

iNOS gene therapy

In mice carrying murine RIF1 fibrosarcoma cells or human HT29 colon carcinoma cells, radiation-induced iNOS gene therapy increased the effectiveness of radiotherapy by the factor 2.0 and 1.3, respectively. This means that 'you could either reduce the radiation dose by 50% and reduce the severity of normal tissue complications, or you could keep the radiation dose the same and you'll have more damage to the tumour cells, equivalent to giving 50% more radiation,' concludes Hirst.

Young finds the philosophy behind the approach attractive, but adds that 'transferring this into patients without some increased efficiency of delivery of the gene would be very difficult.' In the present study, Hirst and colleagues have used liposomes to deliver the iNOS gene. But 'liposomes are very inefficient,' says Young. 'I think you could build this type of system into one of the modern, second- or third-generation viral vectors and evaluate its use then.'

Systemic delivery

Hirst and colleagues are already busy refining their strategy. 'We are doing systemic delivery studies as well as using some other approaches,' hints Hirst. Once they have tweaked the system to satisfaction, this concept will be combined with a whole variety of other things, believes Marie Boyd at the Department of Radiation Oncology, University of Glasgow (http://www.gla.ac.uk). She is currently looking into combining Hirst's system with chemotherapy; other gene therapy groups are now also working with the WAF1 promoter. 'I'm convinced that some aspect of this will be in patients within the next five years,' predicts Boyd.

Reference

1 Worthington, J. *et al*. (2004) Use of the radiation-inducible WAF1 promoter to drive iNOS gene therapy as a novel anti-cancer treatment. *J. Gene Med*. 6, 673–680

1359-6446/04/$ – see front matter PII: S1359-6446(04)03207-6