GLOSSARY

**PHOTOCHEMICAL
INTERNALIZATION (PCI)**

Using photoirradiation and a hydrophilic photosensitizer to enhance the delivery of endocytosed plasmid DNA to the cytoplasm

VENUS REPORTER GENE

A variant of yellow fluorescent protein that can be used to detect cells that express the transfected plasmid DNA

***In vivo* gene transfer by delivery of DNA packaged in a dendrimeric photosensitizer**

Synthetic vectors made of cationic peptides combined with plasmid DNA (pDNA) might enable safer, better targeted and more-efficient means of delivering genes to cells *in vivo* than 'traditional' viral methods. Nishiyama and co-workers developed a targeted method to deliver transgene-containing pDNA, in a complex with positively charged peptides that contain a nuclear localization signal, using light-sensitive chemicals incorporated into a synthetic vector. Following endocytosis of these complexes, the integrity of the endosomal membrane can be further disrupted by photoirradiation, thus giving the plasmid greater access to the nucleus. In their investigation, Nishiyama *et al.* tested whether PHOTOCHEMICAL INTERNALIZATION (PCI) could be used to spatially control transfection *in vivo* through photoirradiation of target sites.

In vitro experiments demonstrated that photosensitization of cells that had endocytosed the vector resulted in increased release of endosomal contents into the cytoplasm, giving pDNA increased access to the nucleus. In addition, PCI increased expression of the transgene over 100-fold, with minimal cytotoxic effects. *In vivo* experiments using a VENUS REPORTER GENE showed that injection of the pDNA complex into subconjunctival tissue of rats' eyes, followed by laser irradiation, resulted in gene expression in the irradiated site in 8/12 eyes.

This is the first report of successful PCI-mediated gene transfer *in vivo*. PCI holds promise for improving drug delivery and gene transfer for the treatment of many diseases, including solid tumors and ophthalmic disease. Spatial control of gene delivery through localized laser treatment should enhance the effectiveness and safety of the procedure.

Kate Matthews

Original article Nishiyama N *et al.* (2005) Light-induced gene transfer from packaged DNA enveloped in a dendrimeric photosensitizer. *Nat Mat* 4: 934–941

Can seizure remission indicate outcome in PNESs?

Psychogenic nonepileptic seizures (PNESs) are paroxysmal episodes that are commonly misdiagnosed as epilepsy. Misdiagnosis can

lead to inappropriate treatment being administered, which can have serious implications. A high proportion of PNES patients become unemployed as a result of their illness and are financially supported through government benefit schemes. These factors have stimulated research into effective treatments, but the psychosocial problems experienced by patients may mean that traditional outcome assessments (based on cessation of seizures) are not relevant. Reuber *et al.* investigated whether seizure remission indicates outcome in PNES patients as it does for epileptic patients.

A questionnaire was sent to the 329 PNES patients who had been diagnosed at Bonn University, Germany between April 1991 and April 2001. Patients were asked to answer questions (from widely used, clinically validated questionnaires) that led to a current psychopathology score and a somatization score. Questionnaires were returned by 164 patients; of the 147 who answered the questions completely enough to be included in analyses, 61 had concurrent epilepsy. Clinical demographics were similar for responders and nonresponders.

Seizures continued in 105/147 patients, but seizure-free status was not a statistically or clinically significant indicator of financial productivity: only 50% of those without seizures had better quality of life and nearly half were unproductive or had continuing psychosocial problems. Only higher educational achievement and younger age at time of the study were statistically significant indicators of seizure-free, financially productive status ($P=0.020$ and $P=0.039$, respectively).

The authors conclude that seizure remission is an unreliable measure of clinical and psychosocial outcome in patients who have experienced PNESs. Controlling seizures should therefore not be the only focus of PNES treatment.

Rebecca Ireland

Original article Reuber M *et al.* (2005) Measuring outcome in psychogenic nonepileptic seizures: how relevant is seizure remission? *Epilepsia* 46: 1788–1795

A novel *parkin* mutation is linked with early-onset PD

Mutations in the *parkin* gene are the most commonly identified cause of autosomal