

## › NEWS UPDATES

### Potential threat from a once-promising therapy

A new study in mice highlights the importance of long-term animal testing in determining the safety of gene therapy strategies.

Patients develop X-linked severe combined immune deficiency syndrome as a result of a defect in the gene for the  $\gamma$  subunit of the interleukin-2 receptor (IL2RG), and a gene therapy strategy using a lentiviral vector to restore proper IL2RG expression seemed like a promising solution. In an initial trial 9 out of 10 patients showed improvement, but it became cause for concern when 3 of them subsequently developed leukemia.

Initially, it was thought that this was a byproduct of improper viral insertion into the host genome. However, Inder Verma and his colleagues at the Salk Institute (San Diego, CA) suggest in a brief communication from the 27 April issue of *Nature* that IL2RG overexpression may be responsible. They show that 18 months after treatment with a lentiviral construct expressing IL2RG, one-third of a test group of mice develop leukemia; however, none of the animals receiving control virus developed disease.

Although IL2RG was not previously seen as a cancer risk, Verma and his colleagues believe that this may be because earlier studies were too limited in duration, and conclude that more extensive preclinical studies should be performed for future gene therapeutic strategies.

### ALS treatment advance

Thalidomide—a drug notorious for causing birth defects—and its analog lenalidomide may slow the progression of amyotrophic lateral sclerosis (ALS), according to research in mice.

ALS, also known as Lou Gehrig's disease, is an incurable neurodegenerative disease affecting ~30,000 Americans at any given time. In ALS patients, degeneration of motor neurons in both the brain and spinal cord leads to muscle wasting, paralysis, and death. The cause of ALS is unknown, but previous studies have suggested that proinflammatory cytokines may cause the nerve cell death seen in ALS.

Now, in a study published in the March issue of the *Journal of Neuroscience*, a research team led by Mahmoud Kiaei of the Weill Medical College of Cornell University (New York, NY) demonstrate in a transgenic mouse model of ALS that both thalidomide and lenalidomide reduced production of the cytokines tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and fibroblast-associated cell surface ligand (FasL) in the lumbar spinal cord. Treated mice showed delayed disease onset, enhanced motor function, slowed weight loss, and increased life span compared with controls.

Researchers think that both compounds reduce TNF- $\alpha$  and FasL levels by destabilizing the TNF- $\alpha$  mRNA. Thalidomide's known teratogenicity should not be a problem, because pregnancy is not likely to be an issue in ALS patients.

### New vaccine protects monkeys from Marburg

A new vaccine given to monkeys following exposure to a lethal dose of Marburg virus prevented hemorrhagic fever caused by this highly lethal relative of the dreaded Ebola virus. If the vaccine proves safe and effective in humans, it could be useful in the protection of caretakers of Marburg patients and lab workers after accidental exposure.

Marburg outbreaks are rare, but the virus kills as many as 90% of those infected. No effective drugs or vaccines exist, and treatment depends on intensive supportive care.

Now, in the 29 April issue of *The Lancet*, researchers at the US Army Medical Research Institute of Infectious Diseases (Fort Detrick, MD, USA) and the Public Health Agency of Canada (Winnipeg, MB, Canada) report the development of a vaccine that protected rhesus macaques when administered 20–30 min after injection of a lethal dose of Marburg virus. The vaccine, which was developed by replacing a surface protein on a harmless virus with a Marburg surface protein, prevented the onset of clinical symptoms in all vaccinated monkeys.

The way in which the vaccine confers protection remains to be determined. Nevertheless, a vaccine that is effective when given after exposure could be a major gain in the event of a random outbreak or biological attack.