Gene therapy in epilepsy

M. Walker

Small molecule approaches to the treatment of epilepsy are effective in about 70% of people but involve “poisoning” body and brain often to treat a limited area of brain tissue, and 30% of people are inadequately treated. For that 30%, resective brain surgery is the most effective approach but involves “destroying” brain tissue with associated deficits and is often limited by proximity to eloquent cortex. Gene therapy offers a novel approach that overcomes many of these problems. It can be targeted to a specific area of brain and to a specific population of neurons. Choosing an appropriate gene enables a modification of the behaviour neurons rather than abolishing their function, so permitting normal, physiological activity. Vector technology has advanced so that it is possible to get genes into neurons effectively and safely. As a result of these advances, we are now on the brink of clinical studies of gene therapy in epilepsy. I will discuss four gene therapy approaches that we have been using: over-expressing an endogenous potassium channel, optogenetics, chemogenetics and an auto-regulatory therapy that responds to glutamate release gene. I will discuss the advantages and disadvantages of each of these and will present a road map from the preclinical studies to first-in-human studies, and explain why such approaches represent the future of epilepsy therapy.