The efficacy of viral mediated gene therapy into brains of sheep affected by neurodegenerative CLN5 Batten disease and translation to humans

Naturally occurring cases of inherited disease in animals provide the genetic basis for analog models of the equivalent human diseases. We study Batten disease (neuronal ceroid lipofuscinoses, NCLs) in sheep. This is a group of rare inherited human neurodegenerative diseases which predominantly affect children. Mutations in any one of 13 different genes may cause the disease and presently effective treatments for any forms are very limited. Sheep are ideal model animals as they have large human-like brains and disease progression closely follows that of affected children.

Our AAV mediated gene therapies into CLN5 affected sheep are yielding results encouraging for translation to humans. A single intraventricular administration of CLN5 gene therapy to pre-symptomatic CLN5 affected sheep brains provided long term protection against stereotypical disease, the only clinical sign being a much delayed-onset loss of vision. A similar administration of CLN5 gene therapy to CLN5 clinically affected sheep yielded similar protection. Traditionally the success of treatments in animal studies has been assessed post mortem, so we have developed a suite of in vivo markers including clinical neurology assessment, volumetric CT scanning and 3D brain reconstructions, MRI studies, maze testing for cognition and vision, and ERG studies to determine the course of blindness. These allow long term longitudinal monitoring of the efficacy of treatments to a natural end-point providing data for translation.

Hosted by Dr Nobuhiko Tokuriki