

## SUMMARY OF THE RELATIONSHIP BETWEEN PRION PROTEIN GENOTYPE AND KURU PHENOTYPE

1. Goldfarb *et al.* (2004)<sup>1</sup> provide an overview of investigations of the effect of codon 129 polymorphisms in the human prion protein (PrP) gene on the phenotype of Kuru. The findings are summarised below.

### Background

2. Kuru is a prion disease of the Fore people of New Guinea. The disease is now almost nonexistent. The origins of Kuru are unclear, but it most likely arose through a spontaneous mutation in the PrP gene of an individual and was then spread laterally through cannibalism. It is believed to have arisen in the early 1900s and it reached epidemic proportions in the 1950s. The Fore adopted endocannibalistic funeral practices where family members were ritually cooked and eaten following their death, with the closest female relatives and children usually consuming the brain. Kuru has largely disappeared because cannibalism has been abolished among the Fore.
3. The clinical presentation of Kuru includes clumsiness, headache, tremor, emotional instability followed by difficulty in moving and eventually patients progressive wasting as a result of failure to swallow or eat. The clinical course ranges from 4-24 months.

### Genotype-phenotype relationship

4. An analysis of the clinical information, together with data on the codon 129 polymorphisms of Kuru cases, suggests that compared with the M/V or V/V genotypes the M/M genotype exhibits:
  - earlier age of onset of clinical symptoms.
  - shorter incubation period.
  - greater susceptibility to infection.
5. Characteristic differences in the neuropathology of Kuru cases early in the epidemic (likely to be M/M) and cases later in the epidemic (likely to be M/V or V/V) also suggest that the pathology of the disease is influenced by PrP genotype.

---

<sup>1</sup> Goldfarb LG, Cervenakova L & Gajdusek DC (2004) Genetic studies in relation to Kuru: an overview. *Curr. Mol. Med.* 4, 375-384.