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SCA19 and SCA22: evidence for one locus with a worldwide distribution

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We read with interest the paper by Ming-Yi Chung and colleagues (Chung *et al*., 2003). In this paper, the authors characterized a four-generation Chinese pedigree with an autosomal dominant phenotype for cerebellar ataxia (ADCA). Their genome-wide linkage study suggested linkage to a locus on chromosome 1p21-q23. The authors stated that the form of ADCA found in this family is distinct from other spinocerebellar ataxias (SCA) and designated this SCA as spinocerebellar ataxia type 22 (SCA22).

However, this locus was previously assigned to SCA19 by the HUGO Gene Nomenclature Committee (http://www.gene.ucl.ac.uk/cgi-bin/nomenclature). Both the clinical features of the affected Dutch ADCA family and the identification of this locus have been extensively described (Schelhaas *et al*., 2001; Verbeek *et al*., 2002). The four-generation Dutch ADCA family has a relatively mild ataxia syndrome with slow progression and additional clinical features, including cognitive impairment, pyramidal signs and peripheral neuropathy (ADCA type I). Genome-wide screening revealed significant linkage with marker D1S534 (maximum lod score 3.82 with $\theta = 00$). The candidate interval spans ~35 cM and is located between the markers D1S1588 and D1S1595. The SCA19 locus has been assigned to the chromosomal region 1p21-q21.

Chung and colleagues report that the candidate SCA22 gene is located between the markers D1S206 and D1S2878. There is significant overlap between the two regions: ~26.9 cM between the markers D1S206 and D1S1595. Although it cannot be excluded that the genes lie in close approximation at this locus, it is more likely that the Dutch and Chinese families suffer from a mutation in the same gene, and that SCA19 and SCA22 represent an identical condition, which should be designated SCA19 as this was the first linkage assigned. By first focusing on CAG repeat-containing genes, both research groups indicated that *KCNN3*, *TNRC4* and *KIAA0467* were the most likely candidate genes. However, CAG expansions in these genes were not found in affected individuals of the Chinese family, and therefore *KCNN3*, *TNRC4* and *KIAA0467* can be excluded as candidate genes. Potassium channel genes (e.g. *KCNJ10*, potassium channel, inwardly rectifying, subfamily J, member ten) are also mapped to this region and were mentioned as serious candidate genes for both SCA19 and SCA22. These genes are of particular interest, because of the presence of myoclonus and tremor in the Dutch SCA19 family.

Unfortunately, Dr Chung and colleagues must have overlooked this earlier assignment. Their excellent work has narrowed the genetic region of interest and suggests that SCA19 is an SCA with worldwide occurrence. The correct assignment of these two families will help clarify the evolving chaos in the genetic classification of these disorders.

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