Key Summary of Conference Abstract

Analysis of the Repeat Size Distribution of over 82,000 Alleles in the Spinocerebellar Ataxias

Background

- Autosomal dominant spinal cerebellar ataxias (SCAs) are a heterogeneous group of inherited neurological conditions characterized by progressive movement disorders.[1]
- More than 35 subtypes of autosomal dominant SCAs have been identified; the most common are caused by expansion of trinucleotide CAG repeats.[1]
- It is not known whether the distribution of repeat sizes is correlated with SCA clinical features or etiology.
- **Objective:** The investigators examined the relationship of repeat expansion size to SCA subtypes in patients tested at a clinical laboratory.

Methods

- Repeat expansion sizes were determined in patient samples (n=82,366) tested for SCAs between 1996 and 2016.
- Distributions of expansion sizes were generated for each SCA subtype: 1, 2, 3, 6, 7, 8, 10, 12, 17, and dentatorubral-pallidoluysian atrophy (DRPLA).
- Repeat expansion sizes were compared to reference ranges published in GeneReviews®.
- Repeat expansion sizes inside (normal size repeats) and outside the reference ranges (borderline repeats) were analyzed.

Results

- Distributions of CAG expansion size fit into 3 patterns:
  - Symmetric, with normal distributions for both normal size repeat and expansion alleles: SCA2, SCA3, and SCA6
  - Skewed, lacking borderline repeats: SCA10, SCA12, and DRPLA
  - Merged, with normal size and borderline repeat alleles together forming a single normal distribution: SCA1, SCA7, SCA8, and SCA17

Conclusion

- Distribution patterns may help identify pathogenic expansion sizes in the SCAs and suggest different mechanisms of repeat expansion.

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Webpage
http://submissions.mirasmart.com/Verify/AAN2017/submission/temp/rad9083F.pdf

Reference

1. Jayadev S, Bird TD. *Genet Med.*2013;15:673-683.