Family-based exome sequencing disclose associated genes in primary headache susceptibility

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INTRODUCTION

- Headaches
  - Primary headaches
    - Migraine
    - Cluster headache (CH)
    - Tension-type headache (TTH)
  - Secondary headaches
- With Aura (MA)
- Without aura (MO)

AIM

To perform a whole-exome sequencing (WES) in Portuguese families to unravel genetic factors in primary headache susceptibility.

SUBJECTS/METHODS

- DNA samples from 3 families (20 individuals) with migraine and CH (as well as controls).
- WES (Novogene corporation)
  - Data analysis: VarAFT (Variant Annotation and Filtration Tool)

RESULTS

- Family 1
  - Rare variants: V3 - SMIT1; V2 - RPL5; V3 - CACNA1A
  - Criteria filters
    - Exonic and splicing variants; UMD Predictor; HPO: Migraine
  - Common variants
    - Exonic and splicing variants; UMD Predictor; HPO: Migraine

  - We can hypothesize that the combination of rare variants in SMIT1, RPL5 and CACNA1A genes could explain the pathophysiological mechanisms of MO disease.

CONCLUSIONS

- For Family 1, we have 2 hypotheses.
  1st hypothesis
  - "Common disease-common variant"?
  2nd hypothesis
  - "Common disease-rare variant"?
    - SMIT1
    - RPL5
    - CACNA1A

- The two types of variants may interplay in migraine susceptibility

- Family 2: A mutation in PRRT2 gene was found associated with MA susceptibility. It was not possible to conclude if this is a de novo mutation or if it was inherited by any of the parents.

- Family 3: results need to be further deepened to draw some conclusions.

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