ORAL PRESENTATION



Open Access

Targeted exon capture and NGS to investigate an undefined myopathy reveal *RYR1* variants

Kathryn Stowell^{1*}, Elaine Langton², Neil Pollock³, Anja Schiemann¹

From 33rd Annual Meeting of the European Malignant Hyperthermia Group (EMHG) Würzburg, Germany. 15-17 May 2014

Background

The family under investigation consists of parents and two daughters, one being the proband. The mother and the proband have elongated facial features. The father and second daughter appear normal. The older daughter presented for elective tonsillectomy aged 8 years. She had severe masseter spasm after suxamethonium. The rest of the procedure was carried out under total intravenous anaesthesia. No blood gas analysis could be done, but a creatine kinase next day was significantly elevated (2934). This led to study of both parents. There was no family history of malignant hyperthermia but an undefined myopathy was suspected in mother and daughter. Both mother and father were diagnosed malignant hyperthermia (MH) susceptible by in vitro contracture test (IVCT). This prompted a DNA analysis for variants associated with MH.

Materials and methods

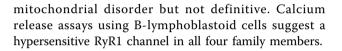
Standard histochemistry, biochemistry and electron microscopy were carried out on muscle tissue from the mother. DNA from all four family members was analysed by targeted exon capture and next generation sequencing using the Ion Torrent platform. B-lymphoblastoid cells were generated from all family members and assayed for abnormal calcium release.

Results

The mother and both daughters carry a premature stop codon in ryanodine receptor subtype 1 (*RYR1*) as well an uncharacterized *RYR1* variant inherited from the father. The mother also carries a second uncharacterized *RYR1* variant, not inherited by either daughter. Muscle histology showed two cox-negative fibres suggestive of a

¹Institute of Fundamental Sciences, Massey University, Palmerston North, 4442, New Zealand

Full list of author information is available at the end of the article



Conclusions

The *RYR1* variants identified cannot be definitively associated with susceptibility to MH, although the functional assays in B-lymphoblastoid cells suggest a hypersensitive channel. It is possible that the undefined myopathy is associated with another gene and the MH susceptible result by IVCT is unrelated to this condition. Further analysis of the family is required for a definitive diagnosis.

Authors' details

¹Institute of Fundamental Sciences, Massey University, Palmerston North, 4442, New Zealand. ²Department of Anesthesiology, Wellington Hospital, Wellington, 6021, New Zealand. ³Department of Anesthesiology, Palmerston North Hospital, Palmerston North, 4410, New Zealand.

Published: 18 August 2014

doi:10.1186/1471-2253-14-S1-A15

Cite this article as: Stowell *et al.*: **Targeted exon capture and NGS to investigate an undefined myopathy reveal** *RYR1* **variants.** *BMC Anesthesiology* 2014 **14**(Suppl 1):A15.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

) Bio Med Central

Submit your manuscript at www.biomedcentral.com/submit



© 2014 Stowell et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (http:// creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.