OMICS International
conferenceseries.com

6th International Conference on

Biomarkers & Clinical Research

August 31-September 02, 2015 Toronto, Canada

Application of clinical exome sequencing and semantic knowledge base approach identifies potential causative variants in a family pedigree with atypical autosomal dominant distal muscular dystrophy

Mahjoubeh Jalali Sefid Dashti[1], Henning F[2], Jeanine Heckmann[1] and **Junaid Gamieldien[1]**
[1]University of the Western Cape, South Africa
[2]Groote Schuur Hospital and University of Cape Town, South Africa

Distal muscular dystrophy (DD) is a group of genetic muscle-wasting disorders resulting in distal muscle weakness. Candidate gene and region approaches have identified several different causative mutations in a number of families with different recent ancestry. Here, we report on novel functional variants that are strong candidates as the genetic cause of a unique form of autosomal dominant DD in a South African family of admixed ancestry. We performed whole exome sequencing in five affected family members and two (one related and one unrelated) controls which identified ~80000 exonic and splicing variants in each targeted exome. As the disease displays an autosomal dominant pattern of inheritance in the family, we hypothesized that the causative mutation was likely to be a novel heterozygous variant. Therefore, in addition to identifying variants shared by the affected members yet absent in the controls, we also filtered out variants seen in the public SNP databases. This resulted in 124 variants that were further filtered based on their potential deleterious impact on the encoded protein or were at a conserved site to arrive at nine functional nsSNPs and four INDELs. As it did not link any of the mutations to known muscular dystrophy genes, our in-house BioOntological Relationship Graph (BORG) semantic database was used to assess their potential indirect links to the disease based on their documented roles in gene functions, pathways and clinical/knockout phenotypes relevant to DD. This variant prioritization strategy resulted in the identification of two novel mutations that are strong candidates for being the cause of the novel autosomal dominant form of DD.

Biography

Mahjoubeh Jalali Sefid Dashti has completed her PhD in the field of Bioinformatics at the South African National Bioinformatics Institute, University of Western Cape and is currently continuing with her Post-doctoral studies at the same Institute. Her research interest lies in biomarker discovery through the application of clinical next generation sequencing in identifying the genetic cause of multifactorial and rare disorders. She is involved in a number of groundbreaking research projects including distal muscular dystrophy, ALS-motor neuron disease, Myasthenia Gravis, post-traumatic stress disorder, maturity onset diabetes of the young and atypical breast cancer in Africans.

mahjoubeh.j@gmail.com

Notes:

J Mol Biomark Diagn
ISSN: 2155-9929 JMBD, an open access Journal

Biomarkers 2015
August 31-September 02, 2015

Volume 6, Issue 4

Page 88