Identification of X-Linked Candidate Disease Genes Through Trio Family Analysis of Family Pedigree

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With thousands of Mendelian-inherited diseases, new bioinformatics technology such as WES has been implemented to identify causal genes and variants within patients. Even with modern technology, analysis of WES sequencing remains difficult for researchers as an individual's exome spans over 30,000 variants with many complex variants. Many variants in X-linked diseases lead to developmental disorders (DD) associated with the brain. In support of using WES to analyze DD-associated Mendelian diseases, a software called Exomiser can be implemented. Exomiser contains multiple filtering, prioritization, and ranking algorithms, making it the ideal software for my partner and me to identify disease-causing variants within-patient(s). We applied Exomiser to a DNA trio (two parents and their child) extracted from CEPH family 1463. The CEPH reference panel serves as the CEU (Central Europe) population of the HapMap project for the generation of a haplotype map of the human genome, making it the ideal basis of research for my partner and me. We have successfully identified multiple DD-associated candidate genes expressed by both the father and son in the trio through Exomiser analysis. Through Exomiser's combined score assessment of 0.95+, we identified five critical genes in relation to DD-associated diseases, including STAG2, IQSEC2, TAF1, NLGN3, and ARSD. Through minimum ranking assessment, we then narrowed down the causal genes to the three top candidate genes STAG2, IQSEC2, and TAF1. All candidate genes identified were expressed in the brain, passed through x-linked inheritance, and ranked as the top causal gene in each patient.

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