Discovery of new genes in Rett syndrome patients by WES

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Objective:

The aim of this project is to discover new candidate genes in a cohort of patients with Rett syndrome phenotype (classic and variants) without genetic diagnosis by whole exome sequencing (WES).

Material and Method:

The patient and healthy parents without genetic diagnosis and negative CGHarray Cytoarray Plus (180K) (Agilent Microarrays) were analyzed by WES with TruSeq Sample Preparation Kit (Illumina). Exomes were captured with TruSeq Exome Enrichment Kit (Illumina) and paired-end 100x2 sequenced with the equip HiScan SQ. The raw data were analyzed in Centre Nacional d'Anàlisi Genòmica (CNAG), in Barcelona, Catalonia, Spain.
The filtering criteria used were: search mutations with 1000g MAF below 0.05 in genes with dominant inheritance, de novo, X-linked, autosomal subject to imprinting and/or with probable functional impact in the CNS.

Results:

Positive genetic diagnosis for 55% of our patients is obtained. The found genes are regulated by MeCP2, attending a RTT-like phenotype. All mutations detected by WES were validated by Sanger sequencing in the index case and their parents.

Conclusions:

We do not only identify 1 gene which causes RTT-like phenotype. For patients with classical Rett without detected mutation, it should be studied the regulatory regions and/or searching for deep intronic mutations in *MECP2* gene. For patients with atypical forms of Rett, it should be analyzed genes related to Rett-like clinics.

Bibliography:

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