عنوان مقاله:

Novel candidate genes in autosomal recessive neurodevelopmental disorders: A three year cohort study

محل انتشار:

اولین همایش علوم پایه دربیماریهای ارثی کودکان (سال: 1398)

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خلاصه مقاله:

Introduction: The progression in diagnosis of neurodevelopmental disorders has undergone considerable in the past decade. In this cohort study we studied over 500 families and aim to explain our broad research on identification of fifteen novel genes (PPP1R21, ADPRHL2, CSF1R, SLC10A7, KIF14, DEAF1, IARS2, CTNS, KLHL24, MFSD2A, DPM3, ADAT3, TUBA3E, HERC1, SLC25A22) on the patients with autosomal recessive neurodevelopmental disordersMaterials & Methods: Families with autosomal recessive pattern compatible with genetic disorders such as seizures, microcephaly, neurodegenerative disorder, progressive brain atrophy, developmental regression have been conducted. A complete clinical and paraclinical examination has been done by expert specialists and clinical geneticist. Genomic DNA was extracted and evaluated through next generation sequencing and followed by bioinformatic analysis. Parents and healthy offspring were assessed for the candidate gene variants.Results: We delineated a novel neurodevelopmental syndrome caused by biallelic PPP1R21 loss of function variants, and identified four previously unreported homozygous truncating PPP1R21 alleles. Pathogenic IARS2 variants have been identified in a number of patients presenting broad clinical phenotypes with autosomal recessive inheritance. By using linkage analysis and exome or genome sequencing, recessive inactivating mutations in ADPRHL2 in six families have been recognized. It has been demonstrated that SLC10A7 mutations reduce SLC10A7 protein expression by in vitro studies. We described the participation of the DEAF1 Gene as potential functional candidates in neurodevelopmental diseases based on computational prediction by using several cellular tools. We have also found genetic variations in

four novel candidate genes such as (NKX6-2, TNR, ACACB, DPM3) based on computational prediction using bioinformatic tools.Conclusion & discussion: The progression in diagnosis of neurodevelopmental disorders has undergone considerable in the past decade, the current focus of our research is on neurodevelopmental disorders, especially autosomal recessive. To further, workup with next generation technologies, using several cellular tools is essential for precise phenotype definition and to understand the underlying disease mechanisms

کلمات کلیدی:

Neurodevelopmental syndrome, Novel genes, neurogenetic, autosomal recessive disorders, progressive disordersRr