



De Novo Missense Mutations in DHX30 Impair Global Translation and Cause a Neurodevelopmental Disorder

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Résumé en anglais	DHX30 is a member of the family of DExH-box helicases, which use ATP hydrolysis to unwind RNA secondary structures. Here we identified six different de novo missense mutations in DHX30 in twelve unrelated individuals affected by global developmental delay (GDD), intellectual disability (ID), severe speech impairment and gait abnormalities. While four mutations are recurrent, two are unique with one affecting the codon of one recurrent mutation. All amino acid changes are located within highly conserved helicase motifs and were found to either impair ATPase activity or RNA recognition in different in vitro assays. Moreover, protein variants exhibit an increased propensity to trigger stress granule (SG) formation resulting in global translation inhibition. Thus, our findings highlight the prominent role of translation control in development and function of the central nervous system and also provide molecular insight into how DHX30 dysfunction might cause a neurodevelopmental disorder.

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Liens

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