# A NOVEL MISSENSE SUBSTITUTION IN *NSUN2* AND A STOP CODON IN *ASPM* CAUSES NEUROLOGICAL DISORDERS IN PAKISTANI FAMILIES

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*During this study, two consanguineous Pakistani families with symptoms of intellectual disability and primary microcephaly were investigated. Affected individuals were born to phenotypically normal parents. Clinical information, including age, sex, age at walking, short stature, microcephaly, behavioral severity, intellectual disability, facial dysmorphism, muscular hypertonia, and the existence of any other illnesses, such as speech delay and epilepsy, was documented. To identify disease-causing variants, whole exome sequencing and subsequent Sanger sequencing were performed. As a result, in one of the families, a novel homozygous missense substitution in the NSUN2 gene and a stop codon in the ASPM gene in the other family were identified. Sequence analysis confirmed a homozygous pathogenic variant (c.1853G>T, p.Arg618Ile) in NSUN2 (NM_017755.6) and a stop codon (c.3978G>A, p.Tryp1326X) in ASPM (NM_018136.5). Our results broadened the mutational spectrum of both genes (NSUN2 and ASPM) causing neurological disorders in the affected individuals of Pakistani families.*

***Key words:*** *NSUN2, ASPM, MRT5, MCPH, intellectual disability, microcephaly.*



## НОВА МІСЕНС-ЗАМІНА В *NSUN2* ТА СТОП-КОДОН У *ASPM* СПРИЧИНЯЮТЬ НЕВРОЛОГІЧНІ РОЗЛАДИ В ПАКИСТАНСЬКИХ РОДИНАХ

Під час цього дослідження було досліджено дві кровноспоріднені пакистанські сім'ї з симптомами інтелектуальної недостатності та первинної мікроцефалії. Хворі особи народилися від фенотипово нормальних батьків. Було задокументовано клінічну інформацію, зокрема, вік, стать, вік початку ходіння, низький зріст, мікроцефалію, тяжкість поведінкових розладів, інтелектуальну недостатність, дисморфію обличчя, м'язову гіпертонію та наявність будь-яких інших захворювань, таких як затримка мовлення та епілепсія. Для виявлення варіантів, що викликають захворювання, було проведено повноекзомне секвенування та подальше секвенування за методом Сангера. В результаті в одній із сімей було виявлено нову гомозиготну місенс-заміну в гені *NSUN2*, а в іншій сім'ї – стоп-кодон у гені *ASPM*. Аналіз послідовності підтвердив гомозиготний патогенний варіант (c.1853G>T, p.Arg618Ile) в *NSUN2* (NM_017755.6) та стоп-кодон (c.3978G>A, p.Tryp1326X) в *ASPM* (NM_018136.5). Наші результати розширили спектр мутацій обох генів (*NSUN2* і *ASPM*), що спричиняють неврологічні розлади у хворих осіб із пакистанських сімей.

***Ключові слова:*** *NSUN2, ASPM, MRT5, MCPH*, інтелектуальна недостатність, мікроцефалія.

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Received May 14, 2025
Received June 17, 2025
Accepted March 18, 2026