



## Therapeutic approaches of hereditary neuropathy disorders and promising gene therapies: a case presentation

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### Abstract:

**Introduction:** Researchers' ever-increasing knowledge of human genes and their disease-associated mutations has inspired new approaches to drug design and discovery. By understanding the molecular mechanisms linked to disease, investigators can better target the activities of the enzymes, intracellular signaling proteins, and transcription factors that regulate disease-associated phenotypes. Recently, biallelic pathogenic variants in PDXK were shown to cause axonal Charcot-Marie-Tooth disease with optic atrophy that responds to PLP supplementation.

**Method:** We performed whole exome sequencing and segregation analysis using Sanger sequencing in order to uncover the pathogenic variant(s) in a family affected by an undiagnosed autosomal recessive peripheral neuropathy. Pathogenicity of the variant was confirmed via enzymatic assays and mass spectroscopy on dried blood-spot samples, derived from all members of the family.

**Result:** Here, we report two affected individuals, from a consanguineous Iranian family presenting with a childhood-onset sensorimotor axonal neuropathy and first signs of optic atrophy. Genetic analysis identified a segregated novel homozygous missense variant in PDXK. We showed that the variant leads to reduced PDXK enzymatic activity with low PLP. The relatively early diagnosis and PLP replacement restored the PLP plasma levels with observable clinical improvement.

**Conclusion:** As this is a rare opportunity for treatment intervention, it is essential that variants in PDXK should be investigated in patients with autosomal recessive, early-onset polyneuropathy, enabling PLP supplementation. Treatment options are still extremely limited, and clear "druggable" pathways are not obvious for many of these mutations. The recent advances in both the understanding of biology and the development of new gene delivery



vectors, gene therapy holds much promise.

### Biography:

Paria Najarzadeh Torbati a Bachelor degree student in Cellular and Molecular Biology, currently works as Research Assistant at Next Generation Genetic PolyClinic, Mashad, Iran. with Dr Ehsan Ghayoor Karimiani, the owner and head of the Lab.

### Publication of speakers:

1. Keller, Natalie & Mendoza Ferreira, Natalia & Maroofian, Reza & Chelban, Viorica & Khalil, Youssef & Mills, Philippa & Boostani, Reza & Najarzadeh Torbati, Paria & Karimiani, Ehsan & Thiele, Holger & Houlden, Henry & Wirth, Brunhilde & Karakaya, Mert. (2020). Hereditary polyneuropathy with optic atrophy due to PDXK variant leading to impaired Vitamin B6 metabolism. *Neuromuscular Disorders*. 30. 10.1016/j.nmd.2020.04.004.
2. Najarzadeh Torbati, Paria. (2018). Exome Sequencing in Diagnosis of Rare Neurogenetic Disorders.
3. Najarzadeh Torbati, Paria. (2018). Genetic Basis of Autism a Neurogenetic complex disease.
4. Najarzadeh Torbati, Paria. (2020). Genetic analysis of rare congenital muscular dystrophy disorders: A three-year cohort study.

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