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Generation of three iPSC lines from fibroblasts of a patient with Cohen syndrome

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Motivation and Aim: Cohen syndrome is a rare autosomal recessive genetic disorder characterized by developmental delay, intellectual disability, microcephaly, neutropenia, dimorphisms, obesity, and ophthalmological and autistic spectrum disorders [1]. It is caused by homozygous or compound heterozygous variants in *VPA13B* gene. More than 200 pathological variants of the *VPS13B* gene in more than 1000 patients are currently registered [2]. The protein is localized on the Golgi complex. It has many domains and the function of some of them is still not clear. VPS13B is involved in lipid transport between cell membranes and is crucial for vesicular trafficking and autophagy. Previously we generated Cohen syndrome patient-specific induced pluripotent stem cells (iPSCs). The iPSC-derived neural stem cells and neurons had numerous ultrastructural abnormalities [3]. In this study, we produced iPSCs from fibroblasts of another Cohen patient that had *VPS13B* gene compound heterozygous variants with unknown clinical significance. A study of unknown variants may clarify the functions of VPS13B as well as the functional roles of its domains.

Methods and Algorithms: Generation and cultivation of the iPSC lines and methods of analysis were described previously [4]. Cell culture was performed at the Collective Center of ICG SB RAS "Collection of Pluripotent Human and Mammalian Cell Cultures for Biological and Biomedical Research" (https://ckp.icgen.ru/cells/; http://www.biores.cytogen.ru/brc_cells/collections/ICG_SB_RAS_CELL) supported by the state project FWNR-2022-0019.

Results: We have generated three iPSC lines from fibroblasts of the Cohen patient with previously unreported compound heterozygous variants (8:g.99766811A>G and 8:g.99859429G>A, HG38). Episomal vectors (Epi5) were used to reprogram fibroblasts. Sanger sequencing confirmed the presence of variants. The cell lines iCS-MCF3-1, iCS-MCF3-3, and iCS-MCF3-5 had normal karyotypes and expressed pluripotency markers OCT4, NANOG, and SSEA-4. Pluripotency was shown by analysis of embryoid bodies; they expressed gene markers of all three germ layers.

Conclusion: These iPSC lines could be used for the study of VPS13B functions and the impact of its variants on the cell function.

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