doi 10.18699/bgrs2024-9.3-10

Generation of iPSCs from a patient with the M694V mutation in the mefv gene associated with familial mediterranean fever and their differentiation into macrophages

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Key words: Familial Mediterranean fever; macrophages; patient-specific induced pluripotent stem cells; differentiation; MEFV gene

Motivation and Aim: Familial Mediterranean fever (FMF) is a systemic autoinflammatory disorder caused by inherited mutations in the *MEFV* (Mediterranean FeVer) gene, located on chromosome 16 (16p13.3) and encoding the pyrin protein. Despite the existing data on *MEFV* mutations, the exact mechanism of their effect on the development of the pathological processes leading to the spontaneous and re-current autoinflammatory attacks observed in FMF, remains unclear. Induced pluripotent stem cells (iPSCs) are considered an important tool to study the molecular genetic mechanisms of vari-ous diseases due to their ability to differentiate into any cell type, including macrophages, which contribute to the development of FMF.

Methods and Algorithms: In this study, we developed iPSCs from an Armenian patient with FMF carrying the M694V, p.(Met694Val) (c.2080A>G, rs61752717) pathogenic mutation in exon 10 of the *MEFV* gene.

Results: As a result, macrophages expressing CD14 and CD45 surface markers were obtained. We found that the morphology of macrophages de-rived from iPSCs of a patient with the *MEFV* mutation significantly differed from that of macrophages derived from iPSCs of a healthy donor carrying the wild-type MEFV gene.

Conclusion: Using patient-specific iPSCs from FMF patients and the CRISPR/Cas9 genome editing system, it will be possible to generate modified isogenic iPSC lines with the corrected mutation, as well as introduce the mutation into control "healthy" iPSCs in the future. Thus, it will be possible to study, on isogenic lines, the contribution of this mutation to changes not only in the morphology, but also in the functional characteristics of macrophages. Such cell platforms will be valuable for understanding the effects of the mutations on pyrin inflammasome dysfunction in FMF.

Funding: The cell reprogramming and characterization was funded by the Ministry of Science and Higher Education of the Russian Federation, Agreement No. 075-15-2021-1063/10. PBMC isolation and molecular-genetic characterization work was supported by the Higher Science and Education Committee of the Ministry of Science, Education,

Culture and Sports of the Republic of Armenia, in the frames of the research project N 21SCG-1F010 and research grant provided by the Armenian Engineers and Scientists of America (AESA, PI: Dr. Roksana Zakharyan). The immunofluorescent imaging was performed using resources of the Common Facilities Center of Microscopic Analysis of Biological Objects, ICG SB RAS (https://ckp.icgen.ru/ckpmabo/, accessed on 13 March 2024), supported by the Budget project of the Institute of Cytology and Genetics (FWNR-2022-0015).

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