Conference Proceedings By

UNITED RESEARCH FORUM
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3rd International Conference on

Cardiology and Cardiovascular Innovations

July 21-22, 2026 | Vienna, Austria

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Cannabidiol differentially regulates cell cycle and metabolism of iPSC-derived cardiac fibroblasts from Duchenne muscular dystrophy patients and healthy controls

Duchenne muscular dystrophy (DMD) is associated with early cardiomyopathy characterized by progressive cardiac fibrosis and heart failure. The endocannabinoid signaling system (ECS) plays an important role in chronic inflammatory and fibrotic conditions and is dysregulated in the skeletal muscle of DMD patients at disease onset and may exacerbate DMD myopathies, since its pharmacological inhibition prevents locomotor impairment in dystrophic mice. Cannabidiol (CBD), a phytocannabinoid with reported modulatory effects on inflammatory and metabolic pathways, has been proposed as a potential therapeutic approach; however, its impact on cardiac fibroblast proliferation and metabolism in DMD remains unclear. This study aimed to evaluate whether CBD regulates cell cycle and metabolic function in human induced pluripotent stem cell (hiPSC)-derived cardiac fibroblasts from DMD patients and healthy controls. hiPSC-derived fibroblasts were treated with CBD at concentrations of 0.1–2 μM, and proliferation was assessed by cell counting. Metabolic function was analyzed using Seahorse extracellular flux assays, including measurements of oxygen consumption rate (OCR) and glycolysis stress tests. Statistical significance was determined using GraphPad Prism 9, with $p < 0.05$ considered significant. CBD treatment significantly increased the number of fibroblasts derived from healthy controls but had no effect on DMD-derived fibroblasts, indicating a genotype-dependent proliferative response. Metabolic analysis revealed that CBD enhanced glycolysis and glycolytic capacity in control cells, whereas glycolytic flux remained unchanged in DMD-derived fibroblasts. No significant changes in basal or maximal mitochondrial respiration or ATP production were observed in either group, suggesting that the differential proliferative response was primarily linked to glycolytic regulation. Together, these data show that CBD differently affects proliferation and glycolysis in hiPSC-derived cardiac fibroblasts depending on genotype, shedding light on metabolic mechanisms underlying altered fibroblast behavior in DMD cardiomyopathy.

Keywords: Duchenne muscular dystrophy, cannabidiol, cardiac fibroblasts.

doi.org/10.51219/URForum.2026.Lesia-Savchenko

ISBN: 978-1-917892-47-6

Biography

Dr. Lesia Savchenko is a postdoctoral researcher at the Institute of Metabolic and Cardiovascular Diseases (I2MC), Toulouse, France. Her research focuses on the role of the endocannabinoid system in cardiac fibroblasts in Duchenne muscular dystrophy using human iPSC-derived models. She earned her PhD in Internal Medicine from Poltava State Medical University, Ukraine.

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ISBN: 978-1-917892-47-6