RESEARCH TOPIC MECM_18

"Treating cardiomyopathy in MERRF syndrome through mitochondrial capture therapy"

Curriculum

MECM Data Science

Research Area

Cardio

Laboratory name

Immunology in Cardiovascular Pathologies Lab

Research Supervisor

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Abstract

This project aims to develop a novel therapeutic strategy for cardiomyopathy associated with MERRF syndrome, a rare mitochondrial disorder caused by mutations in mitochondrial DNA, particularly the 8344A>G mutation. Currently, no effective treatments are available.

The central hypothesis is that transplantation of healthy mitochondria can improve cellular function in affected cardiomyocytes by promoting mitochondrial fusion and reducing the proportion of mutant mitochondrial DNA (heteroplasmy).

To test this hypothesis, the project employs: patient-derived iPSC cardiomyocytes as an in vitro disease model functional assays to evaluate mitochondrial respiration, ATP production, and contractility multi-omics approaches (mtDNA sequencing and RNA sequencing) a MERRF mouse model for in vivo validation. Expected outcomes include improved mitochondrial function, enhanced energy production, and recovery of cardiac function.

Overall, this study aims to demonstrate that mitochondrial transplantation represents a promising therapeutic approach for mitochondrial diseases such as MERRF syndrome.

Main technical approaches

colture cellulari (iPSC → cardiomiociti)
esperimenti di trapianto mitocondriale
test funzionali (ATP, respirazione, contrattilità)
microscopia confocale (mitocondri, fusione)
Seahorse (metabolismo)
ImageJ (analisi immagini)
base di RNA/DNA extraction e sequencing

Scientific references

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2. Chen J, Zhong J, Wang LL, Chen YY. Mitochondrial Transfer in Cardiovascular Disease: From Mechanisms to Therapeutic Implications. Front Cardiovasc Med. 2021;8:771298

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4. Wu YT, Tay HY, Yang JT, Liao HH, Ma YS, Wei YH. Mitochondrial impairment and synaptic dysfunction are associated with neurological defects in iPSCs-derived cortical neurons of MERRF patients. J Biomed Sci. 2023;30(1):70

5. Olkhova EA, Bradshaw C, Blain A, Alvim D, Turnbull DM, LeBeau FEN, et al. A novel mouse model of mitochondrial disease exhibits juvenile-onset severe neurological impairment due to parvalbumin cell mitochondrial dysfunction. Commun Biol. 2023;6(1):1078

Type of contract

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