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Friday

Understanding C9orf72 Hexanucleotide Repeat Linked to Mitochondrial Dysfunction

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State of the art: FTD and ALS are neurodegenerative diseases characterised by declining motor and cognitive functions. Even though these diseases present with distinct sets of symptoms, FTD and ALS are two extremes of the same disease spectrum, and they show considerable overlap in genetic, clinical and neuropathological features. Among these overlapping features, mitochondrial dysfunction is associated with both diseases. Recent studies have shown that cells derived from patient iPSCs display mitochondrial abnormalities, and similar abnormalities have been observed in several animal disease models. A hexanucleotide repeat expansion in the *C9orf72* (C9) gene is the most common genetic cause of both FTD and ALS. *C9orf72* (C9) gene has been linked to mitochondrial abnormalities. This research project will investigate mitochondrial dysfunction in a *Drosophila* C9 model and characterise how mitochondrial genes can modulate C9 toxicity in the *Drosophila* brain.
Methodology: We measured the expression level of Electron Transport Chain components and mitochondrial copy number by qPCR assay. We are characterising mitochondrial function with Oroboros and immunofluorescence stains.
Results: All mitochondrial subunits were significantly downregulated upon C9 induction. We found mitochondrial DNA copy number is decreased in C9 expressing *Drosophila* brains. We are in the process of analysing mitochondrial respiration rates and morphology.
Conclusion: Expression of mitochondrial and nuclear-encoded subunits and mitochondrial DNA copy number is reduced in C9 expressing *Drosophila* brains.

Conflicts of interest

N/A