

Mitochondrial Bioenergetics in Alzheimer's Disease : Insights from the European Synchrotron

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Amphithéâtre SOLEIL

Alzheimer's disease (AD) is increasingly linked to defects in mitochondrial bioenergetics. At the ESRF, we investigate the mechanisms underlying this dysfunction, focusing on respiratory complex I and its assembly factors. Using an integrative approach combining macromolecular crystallography, cryo- electron microscopy, X-ray imaging, and spectroscopy, we reveal novel regulatory mechanisms of energy metabolism, including phosphorylation-dependent modulation at the interface of respiration and fatty acid oxidation. We further demonstrate that AD-related amyloid oligomers disrupt these processes in neuronal mitochondria, contributing to oxidative stress and impaired bioenergetics. These findings highlight how interdisciplinary methodologies advance our understanding of neurodegeneration, offering new perspectives for targeting mitochondrial dysfunction in AD.

[1] Giachin *et al.* Dynamics of Human Mitochondrial Complex I Assembly: Implications for Neurodegenerative Diseases. *Front. Mol. Biosci.* **2016**, *3*:43

[2] McGregor & Soler-Lopez. Structural basis of bioenergetic protein complexes in Alzheimer's disease pathogenesis. *Cur Opin Struct Biol.* **2023**, *80*:102573

[3] Giachin *et al.* Assembly of The Mitochondrial Complex I Assembly Complex Suggests a Regulatory Role for DeFlavination. *Angew. Chem. Int. Ed.* **2021**, *60*(9):4689

[4] McGregor et al. The assembly of the Mitochondrial Complex I Assembly complex uncovers a redox pathway coordination. *Nat Commun.* **2023**, *14*(1):8248



Pause café

Formalités d'entrée : accès libre dans l'amphi du pavillon d'Accueil.

Si la manifestation a lieu dans le Grand Amphi SOLEIL du Bâtiment Central merci de vous munir d'une pièce d'identité (à échanger à l'accueil contre un badge d'accès).

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