DJ-1, a possible therapeutic target against Parkinson’s disease

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Aims

Introduce Parkinson’s disease (PD) and the DJ-1 protein and gene
Study the links between PD, oxidative stress and protein aggregation
Recognize the role of DJ-1 on oxidative stress and protein aggregation
Identify mutations and damage in DJ-1 as cause and risk factors for PD

Parkinson’s disease

- Parkinson’s disease (PD) is the second most common neurodegenerative disorder nowadays
- It consists on dopaminergic neurons cell death through apoptosis
- Patients struggle to start and control voluntary movements
- Sporadic PD → Multifactorial disease
  - Familiar PD → Genetic disease
- Protein aggregation (mainly α-synuclein) and oxidative stress are key factors in patholgy development of PD

Protein aggregation and oxidative stress

- DJ-1 is a 189 amino acid protein, highly expressed in brain as a 40 kDa homodimer
- It has an α/β sandwich folding, belonging to the Pfpl Cysteine proteases family, but spatially distorted catalytic amino acids make it lose protease activity.
- DJ-1 gene location: PARK7, short arm of chromosome 1
- It is 24 kb long and has 8 exons, being exon 1 alternatively spliced

The DJ-1 gene and protein

- DJ-1’s functions on oxidative stress and protein aggregation
  1. Antioxidant: DJ-1 scavenges ROS by oxidizing itself
  2. Glyoxalase: DJ-1 detoxifies aggressive products of energetic metabolism and stabilizes mitochondria
  3. Chaperone: DJ-1 prevents α-syn misfolding and aggregation

Conclusions

- DJ-1 loss of function results in Parkinson’s disease because dopaminergic cells become very sensitive to oxidative stress insults and protein aggregation.
- DJ-1 may be a therapeutic target against Parkinson’s disease. However, further research on its therapeutic potential is needed.

References


Figure 1. Ribbon diagram of the DJ-1 homodimer[1]

Figure 2. Structure of the DJ-1 gene[2]

Figure 3. Mitochondria of paraquat (PQ2+) treated HeLa cells. PQ2+ is a mitochondrial toxin, capable of inducing Parkinsonism.[3]