Clinical collaboration and/or licensing

Repurposing of artesunate for Friedreich ataxia

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The present project and invention relates to the **repurposing of artesunate to treat patients with Friedreich ataxia.**

Friedreich ataxia (FRDA) is a frequent autosomal recessive disease caused by a GAA repeat expansion in the FXN gene encoding frataxin, a mitochondrial protein involved in iron sulfur cluster (ISC) biogenesis. Frataxin deficiency impacts ISC containing proteins and causes an iron accumulation in brain and heart of FRDA patients. Artesunate improves membrane transferrin receptor 1 (TfR1) palmitoylation and decreases iron overload. This paves the road for evidence-based therapeutic strategies at the actionable level of TfR1 palmitoylation in Friedreich ataxia.

Type of project

- Pharmaceutical
- Neurodegenerative disease
- Repurposing

Project highlights

- **Primary indication:** Friedreich ataxia (1/50,000 live births)
- **Repurposing** of artesunate for patients with Friedreich's ataxia
- **Patents:** Methods and pharmaceutical compositions for the treatment of neurodegeneration with brain iron accumulation (WO/2018/115012) priority date 20 December 2016 + 1 additional patent (confidential)
- **Publication:** Petit et al., Reduced CoA pool and secondary transferrin receptor palmitoylation defect trigger iron overload in Friedreich ataxia cultured fibroblasts and peripheral blood mononuclear cells, submitted

Results & roadmap

Results:

- Abnormal cellular iron homeostasis in FRDA fibroblasts induces a massive iron overload in the cytosol and in the mitochondria
- Membrane transferrin receptor 1 (TfR1) accumulation increases TfR1 endocytosis and delayes transferrin recycling and is ascribed to an impaired palmitoylation of TfR1
- Artesunate improves TfR1 palmitoylation and decreases iron overload in FRDA fibroblasts

Next steps:

- A phase I/II study evaluating the safety and efficacy of artesunate in patients with Friedreich ataxia
- Orphan designation expected for the treatment of Friedreich's ataxia

Resources and expertise

- Research team headed by Dr Agnès Rötig with strong expertise in genetics and physiopathological mechanisms associated with mitochondrial diseases
- Collaboration with the French Reference centre for mitochondrial diseases CARAMMEL (head: Pr JP Bonnefont) and the clinical unit of Medical Genetics at Necker Enfants-Malades Hospital
- Ressources: large cohorts, patient samples, genetic tools, cellular models

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