

## Project Title: Sugar Stress in the Brain

**Supervisor:** Hugo Vicente Miranda, Postdoctoral Researcher  
**Co-Supervisor:** Tiago Fleming Outeiro, Full Professor  
CEDOC | NOVA Medical School  
Webpage <http://cedoc.unl.pt/cell-and-molecular-neuroscience/>  
Contact: [hvmiranda@nms.unl.pt](mailto:hvmiranda@nms.unl.pt) | +351-218803101

### Location of research lab/research center:

CEDOC - Chronic Diseases Research Center  
NOVA Medical School / Faculdade de Ciências Médicas  
Universidade Nova de Lisboa  
Rua Câmara Pestana nº 6 | Edifício CEDOC II | 1150-082 Lisboa

### Summary: (1000 characters)

Parkinson's disease (PD) molecular basis is still unclear. Together with aging, it is broadly accepted that the environment plays an important role in PD. Diabetes is considered a pandemic disease and has been suggested as a risk factor for the development of PD. We showed that glycation (a consequence of hyperglycaemia) aggravates the neuronal loss observed in models of PD. However, no clear association between diabetes, hyperglycaemia, glycation and PD has been established.

We hypothesize that protein glycation could alter proteostasis and impair normal neuronal function, ultimately contributing to the onset and progression of PD and other neurodegenerative disorders. We propose to identify neuronal targets of glycation and the pathways involved in the response to glycation. For an establishment of the association between diabetes and PD, we will evaluate the impact of hyperglycemia in models of PD. We will also evaluate glycation defenses as novel therapeutic approaches for PD.

### Bibliographic references:

**2017: Vicente Miranda H, ..., Outeiro TF.** *Glycation potentiates  $\alpha$ -synuclein-associated neurodegeneration in synucleinopathies.* **Brain.** 140 (5): 1399-1419.

**2017: Vicente Miranda H\*, ..., Outeiro TF\*.** *Posttranslational modifications of blood-derived alpha-synuclein as biochemical markers for Parkinson's disease.* **Scientific Reports,** Oct 20, 7:13713.

\* corresponding authors

**2017: Ferreira D, Temido-Ferreira M, Vicente Miranda H, ..., Outeiro TF.**  *$\alpha$ -Synuclein interacts with PrPC to induce cognitive impairment through mGluR5 and NMDAR2B.* **Nature Neuroscience,** Nov, 20(11):1569-1579.

**2017: de Oliveira RM\*, Vicente Miranda H\*, ..., Outeiro TF.** *The mechanism of Sirtuin 2-mediated exacerbation of alpha-synuclein toxicity in models of Parkinson's disease.* **PLoS Biology,** Mar 3;15(3):e2000374. \* equal contribution

**2016: Vicente Miranda H, ..., Outeiro TF.** *Glycation potentiates neurodegeneration in models of Huntington's disease.* **Scientific Reports.** Nov 18; 6:36798.

**2016: Vicente Miranda H, El-Agnaf OM, Outeiro TF.** *Glycation in Parkinson's disease and Alzheimer's disease.* **Movement Disorders.** Jun; 31(6):782-90.

**2010: Vicente Miranda, H, Outeiro, TF,** The sour side of neurodegenerative disorders: the effects of protein glycation, **Journal of Pathology,** 221(1):13-25.