Project Title:

Functional and pathological role of synucleins in retina: from molecular mechanisms to novel therapeutic approaches for retinal neurodegeneration

Supervisor: Sandra Tenreiro, PhD
Institution: CEDOC- Centro de Estudos de Doenças Crónicas, NMS-UNL
Webpage: http://cedoc.unl.pt/cell-and-molecular-neuroscience/
Contact: stenreiro@nms.unl.pt **/phone:** +351 218 803 101

Co-Supervisor: Gabriela Silva, PhD
Institution: CEDOC- Centro de Estudos de Doenças Crónicas, NMS-UNL
Webpage: http://cedoc.unl.pt/gene-therapy/
Contact: gabriela.silva@nms.unl.pt **/phone:** +351 218 803 101

Location of research lab/research center: CEDOC- Centro de Estudos de Doenças Crónicas, NMS-UNL

Summary: (1000 characters)

Diabetic retinopathy (DR) is the leading cause of blindness in working-age adults while Parkinson's Disease (PD) is the most common neurodegenerative movement disorder. Recent evidences point to a common pathophysiology in the visual impairment of PD patients and in DR (1). Disruption of the dopaminergic system was observed in both diseases and may result from loss of dopaminergic amacrine cells (2,3). Dopamine-restoring treatments improve visual symptoms in both PD (4) and diabetic models (5). However, the involved mechanisms are completely unexplored.

Alpha-synuclein (aSyn) aggregation is an hallmark of PD (6). Recently beta-(bSyn) and gamma-synuclein (gSyn) were associated with pathological processes (7,8,9). All syn members are expressed in the retina (10) and form inclusions in the retina from patients with different neurodegenerative diseases (10-14).

Here we aim to:

1) establish correlations between syn profile and retinopathy progression with both diabetes and PD development stages using mouse models;

2) dissect the involved molecular and cellular mechanisms;

3) develop therapeutic approaches for retinal neuroprotection.

Funding: iNOVA4Health 201601-02-014

Bibliographic references:

[1] Tian *et al*., 2015 *Med Hypotheses* **85**,397-8 [2] Chorostecki *et al.* 2015 *J Neurol Sci* **355**,44-8 [3] Gastinger *et al*., 2006 *Invest Ophthalmol Vis Sci*, **47**,3143-50 [4] Bulens *et al*., 1987 *Ann Neurol* **22**,365-9 [5] Aung *et al*., 2014 *J Neurosci* **34**,726-36 [6] Lashuel *et al.,* 2013 *Nat Rev Neurosci* **14**,38-48 [7] Tenreiro *et al*., 2016 Hum Mol Genet. 25:275-90 [8] Taschenberger *et al*., 2013 *Ann Neurol* **74**,109-18 [9] Peters *et al*., 2015 *Ann Clin Transl Neurol* **2**, 29-37 [10] Surguchov *et al*., 2001 *J Neurosci Res* **65**,68-77 [11] Beach *et al*., 2014 *Neurosci Lett*, **571**,34-8 [12] Bodis-Wollner *et al*., 2014 *Ann Neurol* **75**, 964-6 [13] Nguyen *et al*., 2011 *PNAS* **108**, 1176-81 [14] Bohm *et al*., 2013 *Neurobiol Aging* **34**, 2659-75 [15] Greten-Harrison *et al.,* 2010 *PNAS* **107**, 19573-8.