Project Title: Unravelling the role of RNA-binding proteins in Polyglutamine Diseases: from pathogenesis to therapeutics

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Summary: (1000 characters)

The RNA processing events, which are highly regulated by the RNA-binding proteins (RBPs) play a major role in the regulation of brain functioning[1,2]. More than 50% of known RBPs are expressed in the brain and recent studies suggested that a deregulation in RBPs functions and RNA processing events might underlie the pathogenesis of several neurodegenerative diseases (NDs)[3]. The main goal of this project is to investigate the role of RBPs in the context of Polyglutamine (polyQ) diseases and to identify new targets for therapeutic intervention[4,5]. PolyQ diseases are a group of 9 incurable, inherited NDs caused by an abnormal expansion of a CAG tract, having no therapy currently available to stop or delay disease progression. The project will combine high-throughput screening (e.g. transcriptomics of polyQ patients brain samples), *in vitro* models (e.g. neurons derived from polyQ patients iPS cells) and *in vivo* models (e.g. lentiviral and transgenic polyQ mouse models). Importantly, it will be developed in collaboration with the Center for Neuroscience and Cell Biology (Portugal) and the biotech company BrainVectis (France).

Bibliographic references:

[1] Bryant CD, Yazdani N, 2016. RNA-binding proteins, neural development and the addictions. Genes Brain Behav, 15:169-86.
[2] Carmo-Silva, Nóbrega C, Pereira de Almeida L, Cavadas C, 2017, Unravelling the role of ataxin-2 in metabolism. Trends in Endocrinology and Metabolism, 28:309-318
[3] Matos CA, Pereira de Almeida L, Nóbrega C, 2017, Machado-Joseph disease/Spinocerebellar ataxia type 3: from pathogenic mechanisms to therapeutic strategies. Journal of Neurochemistry, *in press*.
[4] Nóbrega C, Carmo-Silva S, Albuquerque D, Vasconcelos-Ferreira A, Vijayakumar U-G, Mendonça L, Hirai H, Pereira de Almeida L, 2015, Reestablishing Ataxin -2 downregulates translation of mutant ataxin-3 and alleviates Machado-Joseph disease. Brain, 138: 3537-54.
[5] Nascimento-Ferreira I*, Nóbrega C*, Ferreira-Vasconcelos A, Onofre I, Albuquerque D, Aveleira C, Hirai H, Déglon N, Pereira de Almeida L, 2013, Beclin-1 mitigates motor and neuropathological deficits in genetic mouse models of Machado-Joseph disease. Brain, 136:2173-88. **equal contribution*