

Implications of miRNAs in several neurodegenerative disorders and their potential as therapeutic interventions

The main objective of my PhD thesis is to identify non-invasive biomarkers (miRNAs) for the detection of sporadic Alzheimer's disease. And using the bioinformatics approach, their potential to interfere with expression of heparin sulphate proteoglycans and proteases, involved in beta amyloid processing will be evaluated.

Moreover, I will try to carry out mRNAs and monoclonal anti-beta amyloid antibody binding (both in blood samples and in mouse tissues) tests, and a cross-test with the Lyme neuroborreliosis, in order to make a wider and differentiated study, and increase the accuracy of the diagnosis protocol. The samples studied will come from patients with dementia diagnosed and classified in 6 groups:

- Control sane subjects (no dementia or mild cognitive impairment diagnosed)
- Alzheimer's disease patients:
 - o Less than 65 years old
 - o Older than 65
- Mild cognitive impairment patients
 - o Less than 65 years old
 - o Older than 65
- Parkinson's disease patients
- Lyme's disease patients

Going deeper in the specific thesis objectives:

- Production of high specific monoclonal antibodies anti-beta amyloid from an hybridoma already selected, and humanization
- Analysis of microRNAs in mice brain tissues by NGS
- Test of monoclonal antibodies anti-beta amyloid in mice tissues
- Analysis of microRNAs in serum samples of patients
- Analysis of mRNAs (transcriptome) in blood samples (both in liposomes and free serum mRNAs) of patients with Alzheimer's Disease by NGS
- Test of monoclonal antibodies anti-beta amyloid in serum samples of patients with Alzheimer's disease
- Cross-test with Lyme disease (ELISAs)

Collaborations:

- For studies with mice I will work at CEDOC, in Faculdade de Ciências Médicas (FCM) da Universidade Nova de Lisboa
- A proteomic profile analysis of the samples will be performed at BIOSCOPE group, in Faculdade de Ciências e Tecnologia (FCT) da Universidade Nova de Lisboa
- Laboratory of Molecular Neuroplasticity and Department of Translational Research of German Center for Neurodegenerative Diseases
- Samples recruitment:
 - o Hospital Garcia de Orta
 - o Instituto Nacional de Saúde Dr. Ricardo Jorge
 - o Faculdade de Ciências Médicas da Universidade Nova de Lisboa