**TITLE:** Mitochondrial DNA and Alzheimer’s disease  

**ABSTRACT**  
In mature neurons, the number of synapses is determined by a neuronal activity-dependent dynamic equilibrium between positive and negative regulatory factors. Likewise, mitochondrial dynamics is regulated by neuronal activity. We hypothesized that Neuronal Pentraxin (NP1), a protein of the mitochondrial program of apoptosis induced by low neuronal activity, could be a negative regulator of synapse density because it is found in dystrophic neurites in Alzheimer’s disease-affected brains. In addition, we hypothesized that the extracellular content of mitochondrial DNA could be a biomarker of neurodegeneration in Alzheimer’s disease. I will present data showing that NP1 negatively regulates excitatory synapse number by modulating neuronal excitability and that NP1 restricts excitatory synaptic plasticity. In addition, I will present data showing that asymptomatic patients at risk of AD, and symptomatic AD patients, but not patients diagnosed with fronto-temporal lobar degeneration (FTLD), exhibit a significant decrease in circulating cell-free mtDNA in the CSF. These findings indicate that activity-dependent regulation of mitochondrial function and mtDNA copy number play a key role in the pathophysiology of Alzheimer’s disease. Support: CIBERNED Grant PI2013/08-3 & SAF2011-23550.  

**PUBLICATIONS**  


