MEASURING OLIGOMERISATION OF TAU HETEROLOGOUSLY EXPRESSED IN YEAST MODELS FOR TAUOPATHIES

J. Van den Brande¹, ², D. Jacobs², P. Grognet², E. Vanmechelen², J. Winderickx¹

¹Functional Biology, Katholieke Universiteit Leuven, Leuven, ²Neurodegenerative Diseases, Innogenetics NV, Zwijnaarde-Gent, Belgium

Introduction: Alzheimer’s disease is characterized by the presence of extracellular senile plaques, composed of Aβ peptide, and intracellular neurofibrillary tangles, which are aggregates of hyperphosphorylated protein tau. Recent studies using in vivo and in vitro models demonstrate that not the end-stage fibrillary deposits of Aβ and tau are toxic but instead the intermediate oligomeric forms of these specific proteins are the potential toxicity mediators. Due to their abnormal structure they can disrupt the normal cellular function (e.g. proteopathy). One of the most powerful models to study the effect of oligomerisation of proteins on cellular function is yeast.

Aims: Since it has been demonstrated that extracellular tau aggregates are taken up by cells and that oligomerisation / aggregation is initiated in the cells, purified tau can be used to study the cellular aspects of extracellular tau-induced aggregation in yeast.

Methods: A yeast model expressing the human tau protein has been demonstrated to express high levels of oligomeric tau forms, as determined by Western-blotting. We now report the further characterization of this model using oligomeric tau sandwich immuno-assays.

Results: We demonstrate that the accumulation of oligomeric tau is dependent on the yeast growth characteristics. Concurrently, we are also able to purify mono- and oligomeric tau from yeast.

Conclusions: Yeast provides us not only with an easily sustainable source of mono- and oligomeric tau, but also allows us to study the fundamental aspect of tauopathies.