Epigenetic Editing of Oxytocin in Alzheimer's Disease

Alzheimer's Disease (AD) is a progressive fatal neurodegenerative disease characterized by neuronal loss, brain atrophy, and cognitive disturbances. Oxytocin is a neuropeptide that has effects on many different processes, such as appetite regulation, empathy, fear, anxiety, and prosocial behaviour. Accumulating evidence suggests that oxytocin also plays a role in memory formation, mainly by maintaining long-term potentiation (LTP). Recently a link between AD-specific DNA methylation signatures and the oxytocin promoter was established in brains of patients suffering from AD, as well as blood from healthy controls, subsequently predicting conversion to AD. The first aim of the project is to examine the effects of oxytocin treatment on AD pathology both *in vitro* and *in vivo*. To that end, APPswe/PS1dE9 mice intranasally treated with oxytocin for a period of 40 days showed cognitive improvement based on a spatial memory task when compared to pre-treatment, indicating that oxytocin can reverse cognitive deficits in a model of familial AD. The second project aim is to investigate the epigenetic signature of the oxytocin promoter in AD and its effect on pathology by means of epigenetic editing. This will be achieved by using CRISPR-dCas9 first *in vitro,* using the murine hippocampal cell line HT22, as well as *in vivo* using APP/PS1 mice.