

Group Name: Functional Epi-Genomics & Cognition and Circuits

IP Name: Jose V Sanchez Mut & Jorge Brotons Mas

Group Web:

(1) <https://in.umh-csic.es/es/grupos/epi-genomica-funcional-del-envejecimiento-y-la-enfermedad-de-alzheimer/>

(2) <https://investigacionuch.ceu.es/grupos/175727/detalle>

Title of the MRP: Psychosis in Alzheimer' disease

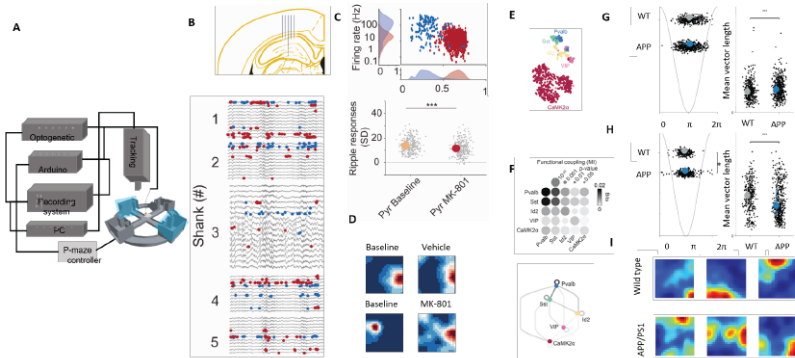
Summary of the MRP: Central nervous system disorders, particularly Alzheimer's disease (AD) and schizophrenia (SCZ), are major biomedical and societal challenges due to their severe impact on cognition and daily functioning. Although AD and SCZ have distinct molecular origins, increasing evidence suggests a common dysfunction of hippocampal–prefrontal circuits, especially those involving inhibitory interneurons and brain oscillations. This Master Research Project will investigate the commonalities between SCZ and AD.

To do so, the student will use a combination of genetic and pharmacological models of AD and SCZ, and characterize their molecular and electrophysiological properties using multielectrode recordings, behavioral tests, and epigenetic techniques. The student is expected to contribute to the analysis of previously recorded electrophysiological and behavioral sessions as well as the generation of new data.

Main objectives include: (i) Description of general electrophysiological properties of AD and SCZ models; (ii) characterization of spatial and memory encoding signatures; (iii) identification of inhibitory motifs in SCZ and AD; and (iv) integration of results with behavioral outputs. The student may also contribute to their molecular characterization, although completion of this aspect is not expected within the duration of the TFM project.

This project aims to advance understanding of the electro-molecular mechanisms underlying psychosis in Alzheimer's disease—an important yet understudied area of research. Psychotic symptoms are among the most distressing manifestations of the disease for patients and families, representing the leading cause of hospital admission, above memory impairment.

Figure 1. Recording setup, electrode implantation, LFP activity, neuronal classification, and altered ripple responses, spatial stability, and firing coordination after MK-801 administration. APP/PS1 preliminary data show theta-modulated pyramidal activity, reduced ripple-phase modulation, and decreased spatial coherence of place cells.



Methods and technology involved in the MRP: The project will use a combination of in vivo electrophysiology, behavioral analysis, optogenetics, molecular biology, epigenetic profiling, and computational approaches in freely behaving animals. Experimental models may include APP/PS1 mice as a model of Alzheimer's disease and MK-801/NMDA receptor Molecular analysis of disease-related and interneuron-associated biomarkers, including genes or proteins linked to synaptic function, inhibitory signaling, neuroinflammation, and neuronal plasticity.

Contact: j.sanchezm@umh.es & jbrotoms@umh.es