- ALZAD SEMINAR -

“Effect of aging on tau pathology propagation in htau mice model of Alzheimer’s disease”

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Alzheimer’s disease (AD) is the most frequent neurodegenerative disease leading to dementia. AD represents a major health challenge for our aging societies. There is currently no efficient therapeutic approach, still due to our limited knowledge of fundamental cellular mechanisms of the disease. The main brain lesions of AD are senile plaques and neurofibrillary tangles (NFTs) which are intraneuronal lesions whose abundance is highly correlated with neuronal loss and the severity of the dementia in AD. NFTs are composed of intraneuronal aggregates of abnormally phosphorylated tau proteins accumulating in a fibrillar structure with twisted filaments called paired helical filaments (PHF-tau). The mechanism of NFT formation is still poorly understood. During disease development, NFT formation follows neuroanatomical pathways suggesting that synaptically connected neurons could transmit tau pathology via the recruitment of normal tau by abnormal tau proteins. Studies have shown that aggregated tau can recruit and seed WT tau protein following intracerebral injections of pathological tau. Tau seeding is transmitted through synaptically connected neurons and composed ofhighly phosphorylated and aggregated tau proteins as in AD. However, even if the propagation of tau pathology could explain the sequential expansion of NFT in Alzheimer’s disease, the mechanism by which the abnormal tau protein can recruit normal tau remains unknown. This study will be devoted to the identification of new targets that are modified when tau pathology propagation occurs and the role of aging on this pathology propagation in AD models. Indeed, aging is the main risk factor for Alzheimer’s disease but its role on the propagation of tau pathology composed of six human WT tau isoforms as found in AD remains unknown.