

Neurophagy laboratory of Prof. Vassiliki Nikolettou

Proposed PhD project:

“Regulation of selective autophagy pathways in the brain”

Macroautophagy, referred to here as autophagy, is a fundamental component of cellular homeostasis, facilitating the lysosomal degradation of superfluous or defective macromolecules and organelles. Recent evidence suggests that autophagy can also subserve the unconventional secretion of proteins, greatly broadening the functional repertoire of this well-conserved mechanism. Recent work from my lab elucidated that in the brain, autophagy has adapted to the physiological needs of neurons. For example, it regulates the turnover of synaptic proteins in response to synaptic plasticity to remodel postsynaptic structures (Kallergi, Daskalaki et al., 2022, Nat. Comm). Moreover, our work delineated the autophagic protein degradome of the brain, revealing the constitutive turnover of protein aggregates, organelles and synapses, via selective autophagy receptor-mediated pathways (Kallergi, Sankar, et al., 2023, Neuron). The aim of the proposed doctoral thesis is to investigate how selective autophagy pathways for protein degradation and protein secretion are regulated in the brain. To this end, we will use interdisciplinary tools, ranging from mouse models to human iPSC-derived brain cells. We will employ state of the art techniques in biochemistry, imaging, electrophysiology, and animal behavioral experiments.