STAVROS NIARCHOS FOUNDATION – FORTH SEMINAR SERIES

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16:00 – 17:00
A. Payatakes Seminar Room

"Autophagy affects neuronal function via cAMP signalling"

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Abstract

Neuronal autophagy is an evolutionarily conserved catabolic process that facilitates recycling of dysfunctional cellular constituents and survival of nerve cells under adverse nutritional conditions. Importance of intact autophagy on neuronal homeostasis preservation is explicitly proven by the severe consequences of its blockage on neuronal survival and functionality: loss of neuronal autophagy causes neuronal pathologies, including neurodegeneration and stroke, while promoting age-related neuronal decline and disease. Apart from the role of basal autophagy on neuronal survival, growing evidence suggests its implication in the development of neuropsychiatric diseases and cognitive impairment in animal experimental models. Relative studies have associated neurodegeneration and certain neuropsychiatric disorders with autophagy impairment, accompanied by extensive protein aggregation. Moreover, autophagy upregulation has been linked to both improvement of neurodegenerative symptoms and mood stabilization in animals. Indeed, evidence suggests that macroautophagy, a specific form of autophagy, plays a major role on presynaptic neurotransmission and neuronal circuits, albeit through unknown mechanisms. Hence, neuronal autophagy is involved in numerous neuronal processes and identification of the relative underlying molecular mechanisms can lead to a better understanding of brain function and neuropsychiatric pathologies in humans. However, the way through which enhancement of neuronal autophagy affects specific brain domains, neuronal circuits, cognition, mood and behaviour is still obscure.

In this study we tested the effects of neuronal autophagic enhancement in flies and zebrafish. Combined behavioral and biochemical analysis revealed that acute and chronic autophagy induction at the brain impaired specific forms of memory and altered behavioral patterns in both species. We identified specific categories of nerve cells at specific brain domains where autophagy exerts its action, serving as coordinators of mood and cognition. We have characterized a neuronal circuit that is affected by autophagy - induced alterations on neurotransmitters transporters' intracellular localisation, which target activity of specific postsynaptic receptors. Such alterations trigger c-AMP signalling activity, responsible for the autophagic effects on behaviour and cognition. Our results indicate that neuronal autophagy affects neuronal functionality through an evolutionary conserved mechanism, which also regulates developmental phenotypes in *Drosophila*.