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Autophagy is differently regulated in astrocytes and microglia exposed to environmental toxic molecules

Cinzia Fabrizi[1], Elena Pompili[1], Viviana Ciraci[1], Paola Lenzi[2], Francesco Fornai[2], Lorenzo Fumagalli[1]

[1] Dipartimento di Scienze Anatomiche, Istologiche, Medico-Legali e dell'Apparato Locomotore, Università Sapienza, Roma, Italy - [2] Dipartimento di Ricerca Traslazionale e delle Nuove Tecnologie in Medicina e Chirurgia, Università di Pisa, Pisa, Italy

Autophagy is generally considered a degradation pathway involved in many neurodegenerative processes. It can be observed in different stress conditions such as starvation generally improving cell survival. Our previous results described the occurrence of autophagy in neuronal cultures exposed to the toxic compound trimethyltin (TMT) (1). TMT belongs to a family of organotin compounds with wide industrial and agricultural applications, especially as heat stabilizers in PVC production and as biocides. In the nervous system TMT determines the selective destruction of neurons in specific brain regions such as the olfactory bulb and the hippocampus.

When this toxic molecule was administered to glial cells we observed in astrocytes a rapid block of the autophagic flux and a consequent increased expression of LC3 and p62 which can be observed both in cultured astrocytes and in the brain of intoxicated animals. Conversely, in microglia autophagy was not impaired in the same conditions and p62 accumulation was not observed neither in vitro primary cultures, nor in brain sections of TMT-treated rats.

The protein p62 (also known as SQTM1) is known to be selectively degraded through autophagy and its accumulation activates the transcription factor Nrf2 by sequestering Keap1 (2).

To note the block of autophagy has been reported to exert an immunosopressive effect in macrophages (3). Thus, the impairment of autophagy in astrocytes could be related to their limited production of pro-inflammatory cytokines and nitric oxide respect to microglia observed after TMT treatment.

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