

P001 The autophagic machinery is necessary for removal of cell corpses during the development of the nervous system.

María Angeles Mellén, Enrique J. de la Rosa and Patricia Boya

*3D Lab (Development, Differentiation & Degeneration),
Department of Cellular and Molecular Physiopathology,
Centro de Investigaciones Biológicas, CSIC. Ramiro de
Maetzu 9, E-28040 Madrid, Spain*

Autophagy is a lysosomal degradative pathway necessary for the clearance of damaged or proteins and organelles. It allows for the recycling of intracellular constituents, providing energy during periods of metabolic stress and thus contributing to cell viability. In addition, disruption of autophagic machinery interferes with embryonic development in several species, although the underlying cellular processes affected remain unclear. Here, we investigate the role of autophagy during the early stages of development of the nervous system by using the chick retina as a model. During these stages of development the retinal neuroepithelium proliferates and starts to generate the first neurons, the retinal ganglion cells. These two developmental processes are accompanied by programmed cell death. We have inhibited the autophagy by using 3-methyladenine and found that retinas accumulated numerous TUNEL-positive cells that correlated with a lack of the “eat-me” signal phosphatidyl-serine. In consequence, neighbouring cells did not engulf apoptotic bodies and persisted as individual cell corpses, a phenotype that was also observed after blockade of phagocytosis with phospho-L-serine. Supplying the retinas with methylpyruvate, a cell-permeable substrate for ATP production, restored ATP levels, phosphatidyl-serine presentation at the cell surface, engulfment and lysosomal degradation of apoptotic bodies. Thus during neurogenesis, the autophagic machinery provides the retina with the energy required for proper cell corpse removal and further degradation of apoptotic cells.