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The mechanism of macroautophagy: The movie

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ABSTRACT

This animated movie presents the mechanism of macroautophagy, hereafter autophagy, by showing the molecular features of the formation of autophagosomes, the hallmark organelle of this intracellular catabolic pathway. It is based on our current knowledge and it also illustrates how autophagosomes can recognize and eliminate selected cargoes.

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Text

Macroautophagy, hereafter autophagy, is a highly conserved intracellular lysosomal degradation process, which is essential to maintain cellular homeostasis by turning over unwanted cytoplasmic structures and recycling their basic components [1]. This catabolic pathway targets excess or dysfunctional proteins, protein complexes and organelles, but also invading pathogens, by sequestering them within double-membrane vesicles called autophagosomes, and delivering them to lysosomes/vacuoles for degradation [2-4]. The interest in autophagy has grown exponentially and attracted the attention of basic and translational researchers, the pharmaceutical industry, but also the public, due to a series of seminal discoveries revealing its involvement in numerous physiological processes and pathological conditions. Autophagy participates in, e.g., the adaptation to starvation and other stresses, development and cell differentiation, and immunity and lifespan extension [5,6]. Moreover, autophagy plays a relevant role in the pathophysiology of neurodegenerative, cardiovascular, chronic inflammatory, muscular and autoimmune diseases, and some malignancies as well [5-8]. More recently, defective autophagy has been implicated in a rapidly expanding group of early onset Mendelian neurodevelopmental and neurological disorders with variable multisystem involvement, the "congenital disorders of autophagy" [9], emphasizing the importance of normally functioning autophagy for neuronal development and maintenance throughout life [10]. Crucially, it has been shown that autophagy modulation is a potentially effective therapy to prevent or cure diseases, including specific types of tumors, muscular dystrophies and neurodegenerative disorders [5,11-13].

Driving next-generation autophagy researchers towards translation (DRIVE) is a pan-European Autophagy researchers' consortium [14]. This Marie Skłodowska-Curie Early Training Network was approved under the European Union's Horizon 2020 Research and Innovation Program and has been funded over a period of 5 years. Within DRIVE, 14 European research teams from academia and industry have trained 15 PhD students through basic, applied, cross-disciplinary and collaborative autophagy research [14]. One of the goals of DRIVE was to create a movie to introduce the mechanistic principles of autophagy to colleagues, students and the general public. Enormous advances in our molecular understanding of autophagy have been made in the past two decades and a visual representation of this cellular pathway makes it possible to easily explain to non-specialists how the field currently thinks about the process of autophagy and how it is currently thought to work. In particular, the movie illustrates how autophagosomes could be generated de novo and how they can specifically recognize and turn over selected

cargoes. With this movie, which can be find at https://www.youtube.com/watch?v=Gc9gx33GvF0, we hope to provide a simple but clear look into autophagy, hopefully conveying our excitement in investigating this unique cellular process that could lead to important medical applications.

Good vision!

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