Commentary: Autophagy and Cell Death

Assembly of early machinery for autophagy induction: novel insights from high resolution microscopy

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: Dynamic association of the ULK1 complex with omegasomes during autophagy induction by Karanasios, J Cell Sci. 2013; 126:5224-38. doi: 10.1242/jcs.132415.

via specifc recognition systems [1].

specifcally cytoplasmic proteins for degradation or it specifcally recognises and eliminates defned cargo, *de novo*

The frst model has given rise to the dominant view when *in vacuo*

live imaging [2, 3]. Instead, autophagosomes form always in association with some pre-existing membrane, be it the ER, mitochondria, Golgi, endosomes or the plasma

For a certain class of autophagosomes, association

Figure 1: A speculative model of early autophagy steps.
of ATG9 vesicles provide a platform for the assembly of ULK1 particles in an ordered arrangement. Such an arrangement is evident in dSTORM images of ER and ATG13, a component of the ULK1 complex (images to the right). The next step during nucleation involves formation of PI3P tubular extensions surrounding ˜ oundisio σ ˢˆ x ᶠ o green). Elongation. Continuous PI3P synthesis, L

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this view, elements of the ULK complex interact with the

structure that very quickly matures into a PI3P-rich

are likely to be extremely complex. Independent EM

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tubular elements [4, 5], whereas similar careful analysis of the omegasome/ER morphology by CLEM has also

and cradling the forming autophagosome [6].

dynamics is what happens at the earliest step which, in both yeast and mammalian cells, depends on the ULK complex and on ATG9 [1]. These early structures are not

techniques and therefore ULK1/ATG9 "assemblies"

"noise". We addressed this problem by establishing that live cells during wide feld imaging can be fxed and re-

way, a newly formed ULK-containing autophagy structure

examined by SIM/dSTORM or by electron microscopy.

properties of the ULK1 complex as it nucleates early

structures, which based on our previous work are devoid of omegasome components [3], are small spherical particles approximately 20-30 nm in diameter and they sit on ER strands, frequently on extensions of the underlying ER. These ULK1 assemblies grow in size by addition of more small particles to a spherical structure of 300 to 400

dSTORM (Figure 1). In whole tomographic reconstitutions of these structures using FIB-SEM it is evident that they

the ER resembling elements of the ERES or ERGIC. Importantly, despite the functional dependence of these structures on ER to Golgi traffc and their morphological resemblance to ERES or to ERGIC they are neither of these pre-existing organelles. Our working hypothesis is

early autophagic machinery generate autophagy-specifc ERES-like sites which then grow into omegasomes by additional membrane re-arrangements and traffc. Given that a small number of ATG9-positive vesicles are always

time mark the ER sites from where they emerge [7], we also hypothesise that a sub-population of ATG9 may somehow mark the ER sites where these early ULK1-positive structures frst coalesce. A speculative model is

ABBREVIATIONS

CLEM (correlative light electron microscopy); dSTORM (direct stochastic optical reconstruction microscopy); ER (endoplasmic reticulum); ERES (endoplasmic reticulum exit sites); ERGIC (endoplasmic reticulum-Golgi intermediate compartment); FIB-SEM (focussed ion beam scanning electron microscopy);