Washington University School of Medicine
Digital Commons@Becker

Open Access Publications

2012

A role for the membrane Golgi protein Ema in autophagy

Sungsu Kim
Washington University School of Medicine in St. Louis

Aaron DiAntonio
Washington University School of Medicine in St. Louis

Follow this and additional works at: https://digitalcommons.wustl.edu/open_access_pubs
Please let us know how this document benefits you.

Recommended Citation
Kim, Sungsu and DiAntonio, Aaron, "A role for the membrane Golgi protein Ema in autophagy." Autophagy. 8, 8. 1269-1270. (2012).
https://digitalcommons.wustl.edu/open_access_pubs/2656

This Open Access Publication is brought to you for free and open access by Digital Commons@Becker. It has been accepted for inclusion in Open Access Publications by an authorized administrator of Digital Commons@Becker. For more information, please contact vanam@wustl.edu.

Autophagy 8:8, 1269–1270; August 2012; © 2012 Landes Bioscience

A role for the membrane Golgi protein Ema in autophagy

Sungsu Kim and Aaron DiAntonio*

Department of Developmental Biology; Washington University School of Medicine; St. Louis, MO USA

©2012 Landes Bioscience. Do not distribute.

Keywords: Ema, Clec16A, Golgi, autophagy, Drosophila, fat body, growth

Submitted: 05/10/12

Revised: 05/21/12

Accepted: 05/24/12

http://dx.doi.org/10.4161/auto.20871

*Correspondence to: Aaron DiAntonio;
Email: diantonio@wustl.edu

Punctum to: Kim S, Naylor SA, Diantonio A. Drosophila Golgi membrane protein Ema promotes autophagosomal growth and function. Proc Natl Acad Sci U S A 2012; 109:E1072–81; PMID:22493244; http://dx.doi.org/10.1073/pnas.1120320109

Autophagy is a cellular homeostatic response that involves degradation of self-components by the double-membraned autophagosome. The biogenesis of autophagosomes has been well described, but the ensuing processes after autophagosome formation are not clear. In our recent study, we proposed a model in which the Golgi complex contributes to the growth of autophagic structures, and that the *Drosophila melanogaster* membrane protein Ema promotes this process. In fat body cells of the *D. melanogaster ema* mutant, the recruitment of the Golgi complex protein Lava lamp (Lva) to autophagic structures is impaired and autophagic structures are very small. In addition, in the *ema* mutant autophagic turnover of SQSTM1/p62 and mitophagy are impaired. Our study not only identifies a role for Ema in autophagy, but also supports the hypothesis that the Golgi complex may be a potential membrane source for the biogenesis and development of autophagic structures.

During development and under stressful conditions, eukaryotic cells undergo a self-digestion process called autophagy. During autophagy, autophagic substrates including mitochondria and protein aggregates are engulfed by double-membraned autophagosomes, which are degraded while interacting with the endocytic compartments such as endosomes and lysosomes. While many details of autophagic membrane trafficking have been studied, it is unclear how the growth and ultimate size of autophagic structures are controlled. In our recent study, we examined autophagy in the *D. melanogaster* fat body cells, which normally display very large autophagic structures. We found a crucial role for *ema* in the growth of autophagic structures. *ema* mutant fat body cells have much smaller autophagic structures than wild type, and this difference is observed within 2 h of autophagy induction.

Given our previous findings that Ema promotes endosomal trafficking in the endocytic *D. melanogaster* Garland cells, the smaller autophagic structures in the *ema* mutant fat body cells could result from impaired fusion between autophagosomes and endosomes and/or lysosomes. However, *ema* mutant's autophagic structures are readily labeled with the endocytic tracer Avidin-Cy3 and the lysosomal marker Lamp1-GFP, indicating that autophagosomes can fuse with endosomes and lysosomes. Live imaging of fat body cells with LysoTracker also confirmed effective acidification of autolysosomes in the *ema* mutant. These results are consistent with the lack of ectopic autophagosomes in the *ema* mutant fat body cells under normal fed conditions, in contrast to many other mutants in the endocytic pathway that display accumulation of immature autophagosomes. Nevertheless, it is possible that autophagosomal fusion with endosomes/lysosomes in the *ema* mutant fat body cells is not completely abolished so that a basal level of autophagy can be operational. However, such a partial loss of function is unlikely to account for the dramatic decrease in the size of autophagic structures in the *ema* mutant.

Ema is a membrane protein that localizes to the Golgi complex in fat body cells in fed conditions. Upon starvation, the Ema protein localizes to the periphery of autophagic structures, consistent with

the model that membrane traffics from the Golgi to autophagosomes and/or autolysosomes. In addition, the *D. melanogaster* Golgi protein Lva, but not the Golgi proteins Gm130 and Grasp, also localizes to the periphery of autophagic structures following induction of autophagy. Importantly, the trafficking of Lva to autophagic structures could not be detected in the *ema* mutant fat body cells. Therefore, we suggest a model in which *ema* promotes the growth of autophagic structures by mediating membrane traffic between the Golgi complex and developing autophagic structures.

Besides the growth of autophagic structures, Ema is also required for wild-type levels of autophagic turnover of the ubiquitin binding protein SQSTM1/p62 and mitophagy. This is somewhat surprising since autophagosomes in the *ema* mutant can mature, fuse with lysosomes and become acidic autolysosomes. Since we have previously demonstrated that *ema* is required for endosomal maturation, this impaired autophagy may be due to defects in the function of endosomes and/or lysosomes. Interestingly, *ema* appears to be dispensable for the autophagosomal engulfing process, since mitochondria are present inside the *ema* mutant autophagosomes. Hence, the defective growth of autophagic structures may stem from a pathway distinct from, and likely later than, the autophagic engulfing process.

What might be the molecular mechanism by which Ema promotes autophagosomal growth? Ema interacts with the membrane-tethering complex HOPS (homotypic fusion and vacuole protein sorting), which has a well-established role in mediating endosomal/lysosomal fusion events. Thus, Ema and the HOPS complex could promote fusion events between autophagosomes and the Golgi complex (or Golgi-derived vesicles). If that is the case, we predict a loss of HOPS function could result in smaller autophagosomes as in the *ema* mutant. Alternatively, the localization of the Ema protein near (and potentially in) the limiting membrane of autophagic structures suggests a potential function for Ema after it arrives at autophagosomes/autolysosomes. For example, the increased number and decreased size of autophagic structures in the *ema* mutant fat body cells at late starvation periods could result from a defect in homotypic fusion between autophagosomes.

In summary, our recent study defines a novel role for the *D. melanogaster* Golgi membrane protein Ema for autophagy. The abnormally small autophagic structures in the *ema* mutant fat body cells imply the existence of a molecular mechanism controlling their growth and ultimate size. Ema is the *D. melanogaster* ortholog of human CLEC16A, a candidate autoimmune susceptibility locus, and we have shown their functions are conserved. Future studies could explore the molecular mechanism of Golgi-to-autophagosome membrane traffic, its relationship to the growth and function of autophagic structures, and its possible link to human disease.

Note

In the original study we used the term "autophagosome" to refer to Atg8-positive structures induced by starvation, which is a more general usage than the common nomenclature. The structures being quantified and colocalized are described in the methods and figure legends and include both autophagosomes and autolysosomes.

©2012 Landes Bioscience. Do not distribute.