AutoClean

Project ID: 769065
Funded under: H2020-EU.1.1. - EXCELLENT SCIENCE - European Research Council (ERC)

Cell-free reconstitution of autophagy to dissect molecular mechanisms

From 2018-06-01 to 2023-05-31, ongoing project

Project details

<table>
<thead>
<tr>
<th>Total cost:</th>
<th>Topic(s):</th>
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<tbody>
<tr>
<td>EUR 1 955 666</td>
<td>ERC-2017-COG - ERC Consolidator Grant</td>
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<thead>
<tr>
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<th>Call for proposal:</th>
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<td>See other projects for this call</td>
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<tr>
<th>Coordinated in:</th>
<th>Funding scheme:</th>
</tr>
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<tbody>
<tr>
<td>Germany</td>
<td>ERC-COG - Consolidator Grant</td>
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Objective

Autophagy, a lysosomal degradation pathway in which the cell digests its own components, is an essential biological pathway that promotes organisational health and longevity and helps combat cancer and neurodegenerative diseases. Accordingly, the 2016 Nobel Prize in Physiology or Medicine was awarded for research in autophagy. Although autophagy has been extensively studied from yeast to mammals, the molecular events that underlie its induction and progression remain elusive. A highly conserved protein kinase, Atg1, plays a unique and essential role in initiating autophagy, yet despite this pivotal importance it has taken over twenty years for its first downstream target to be discovered. However, whilst our identification of the autophagy related membrane protein Atg9 as the first Atg1 substrate is an important advance, the molecular mechanisms that enable the extensive remodelling of cellular membranes that occurs during autophagy is still completely undefined. A detailed knowledge of the inputs and outputs of the Atg1 kinase will enable us to provide a definitive mechanistic understanding of autophagy. We have devised a novel permeabilized cell assay that reconstitutes the pathway in vitro, allowing us to recapitulate key steps in the autophagic process and thereby determine how the individual steps that lead up to autophagy are controlled. We will use this system to dissect the functional role of Atg1 kinase in autophagosome-vacuole fusion (Objective 1), and to determine the origin of the autophagic membrane and the role of Atg1 in expanding these (Objective 2). To reveal how Atg1/ULK1 kinase is activated in mammalian cells, we will apply the unique and carefully tailored synthetic in vivo approaches that we have recently developed (Objective 3). By focusing on the activation of the Atg1 kinase and the molecular events that it executes, we will be able to explain its central role in regulating the autophagic process and define the mechanistic steps in the pathway.

Host Institution

UNIVERSITAETSKLINIKUM FREIBURG
HUGSTETTER STRASSE 49
79106 FREIBURG
Germany

EU contribution: EUR 1 955 666

See on map

Activity type: Higher or Secondary Education Establishments
Contact the organisation
**Beneficiaries**

UNIVERSITAETSCLINIKUM FREIBURG  
HUGSTETTER STRASSE 49  
79106 FREIBURG  
Germany

**EU contribution:** EUR 1 955 666

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Contact the organisation

**To know more**

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