

Rabaptin5 targets autophagy to damaged endosomes and SCVs by interaction with FIP200 and ATG16L1

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Manuscript Source: <https://www.biorxiv.org/content/10.1101/2020.09.01.277764v2>

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- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
- Always consult the original research paper as the true reference source for the text.

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All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title **Rabaptin5 targets autophagy to damaged endosomes and SCVs by interaction with FIP200 and ATG16L1**

S1 [001] Summary

S1 [002] Selective autophagy of damaged organelles is an important process for cellular homeostasis.

Selective autophagy ...
... of damaged organelles is an important process ...
... for cellular homeostasis.

S1 [003] The mechanisms how autophagy selects specific targets is often poorly understood.

The mechanisms how autophagy selects specific targets is often poorly understood.

S1 [004] Rabaptin5 was previously known as a major regulator of early endosome identity and maturation.

Rabaptin5 was previously known ...
... as a major regulator ...
... of early endosome identity ...
... and maturation.

S1 [005] Here we identified two novel Rabaptin5 interactors: FIP200, a subunit of the ULK1 autophagy initiator complex, and ATG16L1, a central component of the E3-like enzyme in LC3 lipidation.

Here we identified two novel Rabaptin5 interactors: ...
... FIP200, ...
... a subunit ...
... of the ULK1 autophagy initiator complex, ...
... and ATG16L1, ...
... a central component ...
... of the E3-like enzyme ...
... in LC3 lipidation.

S1 [006] Indeed, autophagy of early endosomes damaged by chloroquine or monensin treatment was found to require Rabaptin5 and particularly a specific short sequence motif binding to the WD domain of ATG16L1.

Indeed, ...
... autophagy ...
... of early endosomes damaged ...
... by chloroquine ...
... or monensin treatment was found ...
... to require Rabaptin5 ...
... and particularly a specific short sequence motif binding ...
... to the WD domain ...

... of ATG16L1.

S1 [007] Rabaptin5 and this interaction with ATG16L1 is further required for much of autophagic elimination of Salmonella enterica in phagosomes with early endosomal characteristics early after infection.

Rabaptin5 ...
... and this interaction ...
... with ATG16L1 is further required ...
... for much ...
... of autophagic elimination ...
... of Salmonella enterica ...
... in phagosomes ...
... with early endosomal characteristics early ...
... after infection.

S1 [008] Our results demonstrate a novel function of Rabaptin5 in quality control of early endosomes in the selective recruitment of autophagy to damaged early endosomes and phagosomes.

Our results demonstrate a novel function ...
... of Rabaptin5 ...
... in quality control ...
... of early endosomes ...
... in the selective recruitment ...
... of autophagy ...
... to damaged early endosomes ...
... and phagosomes.

S2 [009] INTRODUCTION

S2 [010] Endosomes are dynamic organelles that receive endocytic cargo from the plasma membrane and exocytic material from the trans-Golgi for sorting to late endosomes and lysosomes, to the cell surface via recycling endosomes, or back to the Golgi (Naslavsky and Caplan, 2018).

Endosomes are dynamic organelles ...
... that receive endocytic cargo ...
... from the plasma membrane ...
... and exocytic material ...
... from the trans-Golgi ...
... for sorting ...
... to late endosomes ...
... and lysosomes, ...
... to the cell surface ...
... via recycling endosomes, ...
... or back ...
... to the Golgi ...
... (Naslavsky ...
... and Caplan, 2018).

S2 [011] Endosomal identities are defined by specific Rab GTPases, their effectors, and characteristic phosphoinositides.

Endosomal identities are defined ...
... by specific Rab GTPases, ...
... their effectors, ...
... and characteristic phosphoinositides.

S2 [012] At early endosomes, Rab5 is the hallmark GTPase that activates VPS34/p150 to produce phosphatidylinositol-3-phosphate (PI3P) and recruits early endosome antigen 1 (EEA1) and Rabenosyn-5, two multivalent PI3P-binding proteins that act as membrane tethers to mediate homotypic endosome fusion.

At early endosomes, ...
... Rab5 is the hallmark GTPase ...
... that activates VPS34/p150 ...
... to produce phosphatidylinositol-3-phosphate ...
... (PI3P) ...
... and recruits early endosome antigen 1 ...
... (EEA1) ...
... and Rabenosyn-5, ...
... two multivalent PI3P-binding proteins ...
... that act ...
... as membrane tethers ...
... to mediate homotypic endosome fusion.

S2 [013] Rab5-GTP and PI3P are also responsible for recruitment of the Mon1/Ccz1 complex to activate Rab7 and deactivate Rab5 in the process of Rab conversion during maturation from early to late endosomes (Huotari and Helenius, 2011; Poteryaev et al., 2010).

Rab5-GTP ...
... and PI3P are also responsible ...
... for recruitment ...
... of the Mon1/Ccz1 complex ...
... to activate Rab7 ...
... and deactivate Rab5 ...
... in the process ...
... of Rab conversion ...
... during maturation ...
... from early ...
... to late endosomes ...
... (Huotari ...
... and Helenius, 2011; ...
... Poteryaev et al., 2010).

S2 [014] Rab5 activity is regulated by a complex of Rabaptin5 and Rabex5, the GDP/GTP exchange factor of Rab5.

Rab5 activity is regulated ...
... by a complex ...
... of Rabaptin5 ...
... and Rabex5, ...
... the GDP/GTP exchange factor ...
... of Rab5.

S2 [015] Rabaptin5 binds to Rab4-GTP and Rab5-GTP, and Rabex5 binds to ubiquitin to mediate membrane recruitment and to activate Rab5 on early endosomes (Kälin et al., 2016; 2015; Mattera and Bonifacino, 2008; Mattera et al., 2006).

Rabaptin5 binds ...
... to Rab4-GTP ...
... and Rab5-GTP, ...
... and Rabex5 binds ...
... to ubiquitin ...
... to mediate membrane recruitment ...
... and to activate Rab5 ...
... on early endosomes ...
... (Kälin et al., 2016; ...
... 2015; ...
... Mattera ...
... and Bonifacino, 2008; ...
... Mattera et al., 2006).

S2 [016] Searching for new interactors of Rabaptin5, we performed a yeast two-hybrid screen and discovered as a novel binding partner FIP200, a component of the ULK1–FIP200–ATG13–ATG101 autophagy initiator complex.

Searching ...
... for new interactors ...
... of Rabaptin5, ...
... we performed a yeast two-hybrid screen ...
... and discovered ...
... as a novel binding partner FIP200, ...
... a component ...
... of the ULK1–FIP200–ATG13–ATG101 autophagy initiator complex.

S2 [017] Autophagy is a self-degradative survival mechanism of eukaryotic cells important to preserve cellular homeostasis in response to stress conditions such as lack of nutrients, accumulation of misfolded or aggregated proteins, damaged organelles, and pathogen infection (Bento et al., 2016; Dikic and Elazar, 2018; Mercer et al., 2018; Morishita and Mizushima, 2019).

Autophagy is a self-degradative survival mechanism ...
... of eukaryotic cells important ...
... to preserve cellular homeostasis ...
... in response ...
... to stress conditions ...
... such as lack ...
... of nutrients, ...
... accumulation ...
... of misfolded ...
... or aggregated proteins, ...
... damaged organelles, ...
... and pathogen infection ...
... (Bento et al., 2016; ...
... Dikic ...
... and Elazar, 2018; ...
... Mercer et al., 2018; ...

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