

Response to reviewers

We thank the editors and reviewers for valuable comments and advice.

The changes based on their advice are highlighted in revised form of this manuscript.

Here we address the comments of reviewers:

1- Reviewer's code: 03253495

We thank the reviewer for accepting our manuscript in its current form.

2- Reviewer's code: 02533177

The suggested reference (reference 23) was added based on his advice and highlighted: **23 Bernardini JP, Lazarou M, Dewson G. Parkin and mitophagy in cancer. *Oncogene* 2016 Sep 5. doi: 10.1038/onc.2016.302. [Epub ahead of print].**

3- Reviewer's code: 03552346

We thank the reviewer for accepting our manuscript in its current form.

4-Reviewer's code: 02543991

Based on valuable advice of the reviewer, we added additional sentences and one reference (highlighted) showing examples of KRAS-driven tumors. The sentences are: KRAS mutant pancreatic adenocarcinoma has been reported to rely on autophagy and mitophagy to supply bioenergetic intermediates for the TCA cycle. Mitophagy appears also to be a prosurvival mechanism in immortal baby mouse kidney epithelial cells ectopically expressing oncogenic HRAS or KRAS by removing damaged mitochondria ^[9].

The reference is: **9 Bryant KL, Mancias JD, Kimmelman AC, Der CJ. KRAS: feeding pancreatic cancer proliferation. *Trends Biochem Sci*; 2014; 39:91-100.**

5-Reviewer's code: 03547833

We thank the reviewer for valuable comments. We added sentences highlighted related to details of Parkin-mediated mitophagy, the roles of Atg-5,7 and expansion of PCNA based on advice.

1-Regarding details of mitophagy, we added these sentences: **Parkin-**

mediated ubiquitination of OMM proteins stimulates the recruitment of different LC3 interacting region (LIR)-containing autophagy receptors which bind ubiquitin-tagged OMM proteins, including p62, optineurin and NBR1

2-Regarding Atgs-5,7, we added these sentences: Upon autophagy activation the Atg4 cysteine protease first cleaves pro-LC3 at the C-terminus, thus forming LC3-I. Induction of Atg7 conjugates phosphatidylethanolamine (PE) to LC3-I, forming LC3-II (essential form of LC3 for mitophagosome formation). The Atg5/12/16 complex also acts as an E3 ligase, promoting PE conjugation to LC3

3- PCNA was expanded to: proliferating cell nuclear antigen

Thank you

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