Author's Accepted Manuscript

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PII: S0014-4827(18)30420-8
DOI: https://doi.org/10.1016/j.yexcr.2018.07.013
Reference: YEXCR11117

To appear in: *Experimental Cell Research*

Received date: 2 May 2018
Revised date: 4 July 2018
Accepted date: 6 July 2018

Cite this article as: Wei Sun and Jianbo Yue, TPC2 mediates autophagy progression and extracellular vesicle secretion in cancer cells, *Experimental Cell Research,* https://doi.org/10.1016/j.yexcr.2018.07.013

TPC2 mediates autophagy progression and extracellular vesicle secretion in cancer cells

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Abstract

Autophagy is an evolutionarily conserved lysosomal degradation process, and is involved in various cellular processes. Here we studied the role of two pore channel 2 (TPC2), a lysosomal non-selective Na^+/Ca^{2+} channel, in autophagy progression. We found that TPC overexpression in 4T1 mouse breast cancer cell line or in HeLa human cervical cancer cell line inhibited the fusion between autophagosome and lysosome, resulting in the accumulation of autophagosomes accompanied with increased lysosomal pH and TFEB nuclear localization. Interestingly, we also found that extracellular vesicle (EV) secretion was markedly decreased in TPC2 overexpressing cells but was induced in TPC2 knockdown cells. In addition, migration of TPC2 knockdown cells, not TPC2 overexpressing cells, was inhibited. Taken together, these results support a role of TPC2 in autophagy progression and EV trafficking in cancer cells.

Keywords: TPC2, autophagy, lysosome, extracellular vesicle