ACTIVITY REPORT



Private Universities (2014-2018)

Roles of Membrane Contact Sites in Organelle Dynamics and Diseases

Elucidation of the roles of syntaxin 17 localized in the mitochondria-associated membrane (MAM) and its participation in MAM-associated diseases



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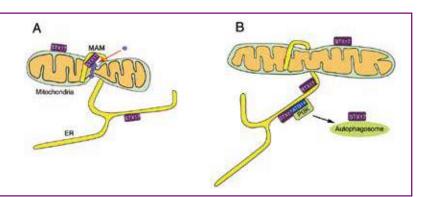
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Research summary

The endoplasmic reticulum (ER) contains various subdomains that are in contact with other organelles. The ER subdomain facing mitochondria is called the mitochondria-associated membrane (MAM). The MAM regulates mitochondrial activity through Ca²+ and synthesizes lipids in cooperation with mitochondria. Accumulating data have disclosed that the ER-mitochondria interface is the site for various important cell functions, beyond Ca²+ homeostasis and lipid synthesis. Moreover, the close relationship between this site and neurodegenerative diseases has been pointed out. In this project, we will explore the roles of syntaxin 17 (STX17) in the ER-mitochondria interface and MAM-associated diseases.

Figure

Different roles of STX17 in response to cellular physiology. (A) In fed cells, STX17 promotes mitochondrial fission by regulating Drp1 (represented by D in blue circle) localization/activity. (B) In starved cells, STX17 switches its binding from Drp1 to the PI3K subunit ATG14, leading to mitochondrial elongation and autophagosome formation. This elongation allows mitochondria to escape from autophagic degradation.



References

- 1.Arasaki K, Shimizu H, Mogari H, Nishida N, Hirota N, Furuno A, Kudo Y, Baba M, Baba N, Cheng J, Fujimoto T, Ishihara N, Ortiz-Sandoval C, Barlow LD, Raturi A, Dohmae N, Wakana Y, Inoue H, Tani K, Dacks JB, Simmen T, *Tagaya M. (2015) Developmental Cell. 32:304-317.
- 2.Noda C, Kimura H, Arasaki K, Matsushita M, Yamamoto A, Wakana Y, Inoue H, *Tagaya, M. (2014) Valosin-containing protein-interacting membrane protein (VIMP) links the endoplasmic reticulum with microtubules in concert with cytoskeleton-linking membrane protein (CLIMP)-63. *Journal of Biological Chemistry*. 289:24304-24313.
- 3.*Tagaya M, Arakaki K, Inoue H, Kimura H. (2014) Moonlighting functions of the NRZ (mammalian Dsl1) complex. Frontiers in Cell and Developmental Biology. 2:25.
- 4.He S, Ni D, Ma B, Lee JH, Zhang T, Ghozalli I, Pirooz SD, Zhao Z, Bharatham N, Li B, Oh S, Lee WH, Takahashi Y, Wang HG, Minassian A, Feng P, Deretic V, Pepperkok R, <u>Tagaya M</u>, Yoon HS, *Liang C. (2013) PI(3)P-bound UVRAG coordinates Golgi-ER retrograde and Atg9 transport by differential interactions with the ER tether and the Beclin1 complex. *Nature Cell Biology* 15:1206-1219.
- 5.Arasaki K, Takagi D, Furuno A, Sohda M, Misumi Y, Wakana Y, Inoue H, *Tagaya M. (2013) A new role for RINT-1 in SNARE complex assembly at the trans-Golgi network in coordination with the COG complex. *Molecular Biology of the Cell*. 24:2907-2917.
- 6.Wakana Y, Villeneuve J, van Galen J, Cruz-Garcia D, <u>Tagaya M</u>, *Malhotra, V. (2013) Kinesin-5/Eg5 is important for transport of CARTS from the trans-Golgi network to the cell surface. *Journal of Cell Biology*, 202:241-250.