Cell. Mol. Life Sci. (2013) 70:3041–3043
DOI 10.1007/s00018-013-1271-y

Cellular and Molecular Life Sciences

ERRATUM

Erratum to: Control of cell growth: Rag GTPases in activation of TORC1

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Published online: 1 February 2013

Erratum to: Cell Mol Life Sci
DOI 10.1007/s00018-012-1195-y

Unfortunately, the original publication of this paper contained errors in the presentation of Figs. 1 and 2. The corrected figures are given below.

The online version of the original article can be found under doi:10.1007/s00018-012-1195-y.

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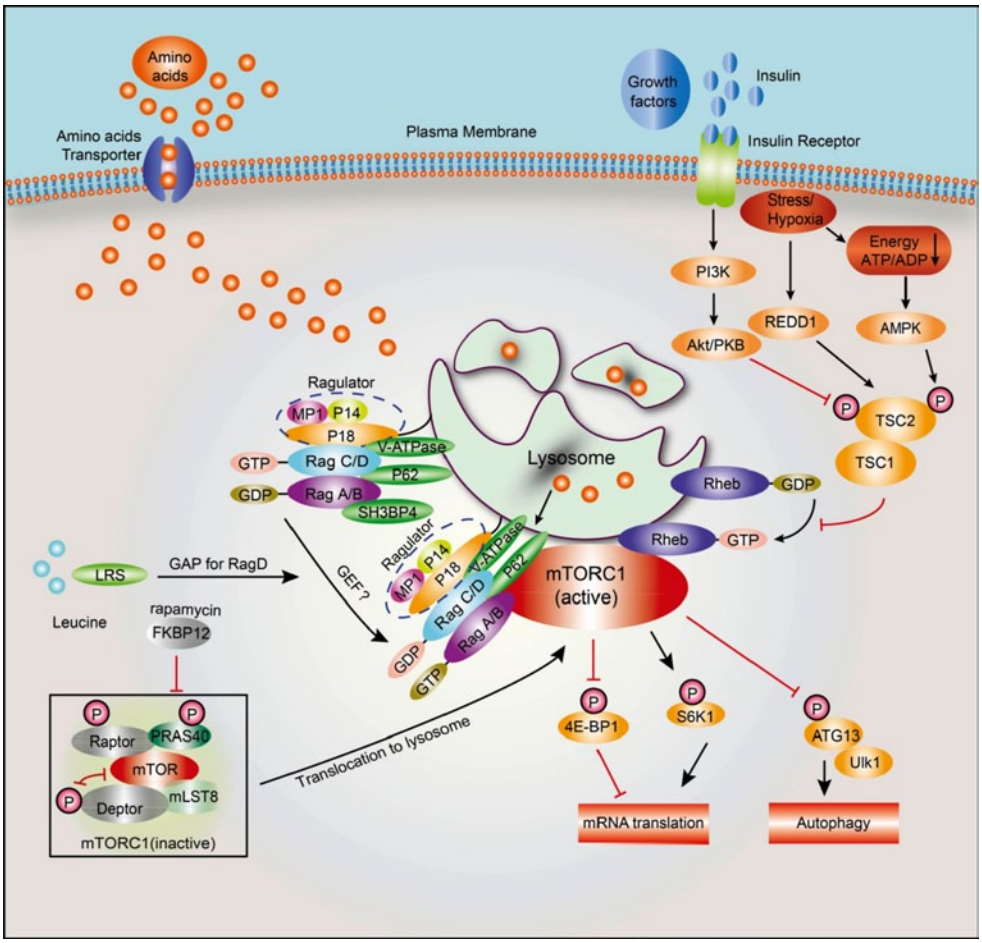

Fig. 1 Rag GTPases in activation of mTORC1 signaling pathway in mammals. The mammalian target of rapamycin complex 1 (mTORC1) is a central regulator controlling cell growth through integrating signals from growth factors, cellular energy levels, stress, to amino acids. mTORC1 promotes mRNA translation by phosphorylation of S6K1 and 4E-BP1 and inhibits autophagy by phosphorylation of ATG13 and Ulk1. Growth factors stimulate mTORC1 through phosphorylation and inactivation of TSC1/2 complex. Akt phosphorylates TSC2 and inactivates the GAP activity of TSC1/2, leading to the activation of Rheb, which is essential for mTORC1 activation. AMPK is activated when cells are exposed to low energy (low ATP:ADP ratio). Stresses inhibit mTORC1 in part by reducing cellular ATP levels and leading to AMPK activation. Hypoxia also induces the expression of DNA damage response 1(REDD1), which activates TSC1/2 and inhibits mTORC1. Activated AMPK phosphorylates TSC2 and leads to activation of TSC1/2 GAP activity, Rheb inhibition, and mTORC1 inactivation. Rag GTPases play a central role in amino acid-induced mTORC1 activation. Rag GTPases form heterodimers and are localized on the late endosomal or lysosomal surface through the interaction with Ragulator complex (p18/MP1/p14). The heterodimerization of Rag GTPases does not depend on amino acids, whereas the nucleotide loading status of Rag GTPases is regulated by amino acids through proteins as indicated. LRS is a leucine sensor and functions as a GAP for RagD GTPase to stimulate mTORC1 activity. Moreover, amino acid accumulation in lysosomal lumen promotes v-ATPase-mediated regulation of nucleotide loading on Rag GTPases. Active Rag GTPase heterodimers (RagA/B^{GTP}-RagC/D^{GDP}) work together with Ragulator and v-ATPases to recruit mTORC1 to the lysosomal surface where Rheb is localized for mTORC1 activation. Adaptor protein p62 interacts with Rag GTPases to form a complex distinct from Ragulator-Rag, and may recruit mTORC1 to lysosomal surface for activation. SH3BP4 is a negative regulator of Rag GTPase, which prevents active Rag GTPases formation through interaction with $RagA^{GDP}$, and thereby inhibits the interaction between Rag GTPases and Raptor for mTORC1 activation

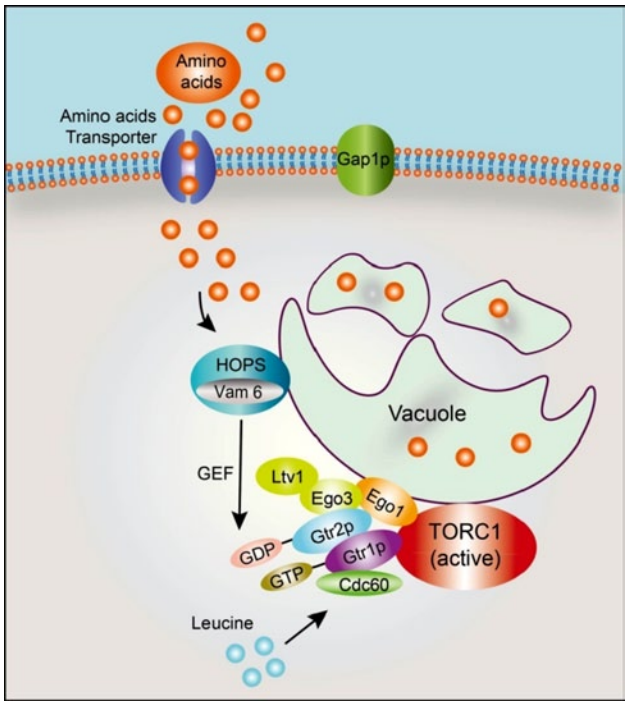

Fig. 2 Amino acid-induced TORC1 activation in yeast. Gtr1p and Gtr2p in yeast are orthologs of mammalian Rag A/B and Rag C/D GTPases, respectively. $Gtr1p^{GTP}$-$Gtr2p^{GDP}$ forms an active heterodimer to mediate amino acid-induced TORC1 activation. $Gtr1p^{GTP}$-$Gtr2p^{GDP}$ heterodimer interacts with Ltv1, Ego1, and Ego3, and forms an EGO/GSE complex, which is localized to the vacuole surface via N-terminal myristoylation of Ego1. Vam6 interacts with Gtr1p and functions as a GEF for Gtr1p. Cdc60, a leucine sensor, binds to $Gtr1p^{GDP}$ and prevents GTP from hydrolysis, and therefore activates TORC1