Activation of the RAS/cyclic AMP pathway suppresses a TOR deficiency in yeast

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The TOR (target of rapamycin) and RAS/cyclic AMP (cAMP) signaling pathways are the two major pathways controlling cell growth in response to nutrients in yeast. In this study we examine the functional interaction between TOR and the RAS/cAMP pathway. First, activation of the RAS/cAMP signaling pathway confers pronounced resistance to rapamycin. Second, constitutive activation of the RAS/cAMP pathway prevents several rapamycin-induced responses, such as the nuclear translocation of the transcription factor MSN2 and induction of stress genes, the accumulation of glycogen, the induction of autophagy, the down-regulation of ribosome biogenesis (ribosomal protein gene transcription and RNA polymerase I and III activity), and the down-regulation of the glucose transporter HXT1. Third, many of these TOR-mediated responses are independent of the previously described TOR effectors TAP42 and the type 2A-related protein phosphatase SIT4. Conversely, TOR-controlled TAP42/SIT4-dependent events are not affected by the RAS/cAMP pathway. Finally, and importantly, TOR controls the subcellular localization of both the protein kinase A catalytic subunit TPK1 and the RAS/cAMP signaling-related kinase YAK1. Our findings suggest that TOR signals through the RAS/cAMP pathway, independently of TAP42/SIT4. Therefore, the RAS/cAMP pathway may be a novel TOR effector branch.

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