EIF2AK4 (GCN2) binds tRNA

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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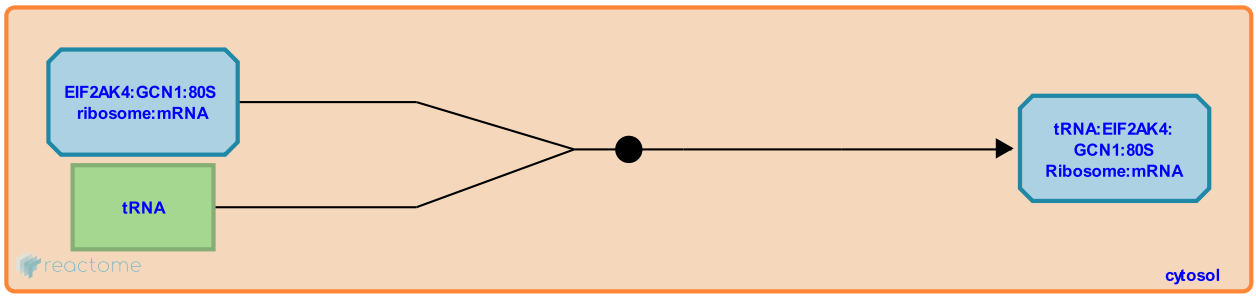
EIF2AK4 (GCN2) binds tRNA ↗

Stable identifier: R-HSA-9633005

Type: binding

Compartments: cytosol

Inferred from: Eif2ak4 binds tRNA (Mus musculus), GCN2 binds tRNA (Saccharomyces cerevisiae)



The histidyl-tRNA synthetase-like domain of EIF2AK4 (GCN2) binds uncharged tRNA, resulting in activation of the protein kinase domain of EIF2AK4 (Inglis et al. 2019 and inferred from yeast homologs and mouse homologs). In the absence of tRNA, EIF2AK4 appears to exist in an equilibrium between antiparallel and parallel dimers. Upon binding tRNA, the parallel dimer is stabilized and the C-terminal domain shifts away from the protein kinase domain, resulting in activation of the kinase activity of EIF2AK4 (inferred from GCN2, the yeast homolog).
EIF2AK4 interacts with GCN1 and the P-stalk of ribosomes (Inglis et al. 2019), though the interaction between mammalian EIF2AK4 and ribosomes is not as stable as the interaction between yeast GCN2 and ribosomes (inferred from yeast homologs and mouse homologs). By such transient interactions, a population of EIF2AK4 may sample a larger population of ribosomes for uncharged tRNAs. The interaction between EIF2AK4 and GCN1 is required for efficient phosphorylation of EIF2S1 by EIF2AK4 and GCN1 may act to transfer uncharged tRNAs from the A site of the ribosome to EIF2AK4 (inferred from yeast homologs and mouse homologs).

Literature references

Hegde, RS., Perisic, O., Masson, GR., Inglis, AJ., Shao, S., McLaughlin, SH. et al. (2019). Activation of GCN2 by the ribosomal P-stalk. *Proc. Natl. Acad. Sci. U.S.A., 116*, 4946-4954. ↗

Editions

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