

# p-T899-EIF2AK4 (GCN2) phosphorylates

## EIF2AS1

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02/10/2024

## 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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 89

This document contains 1 reaction ([see Table of Contents](#))

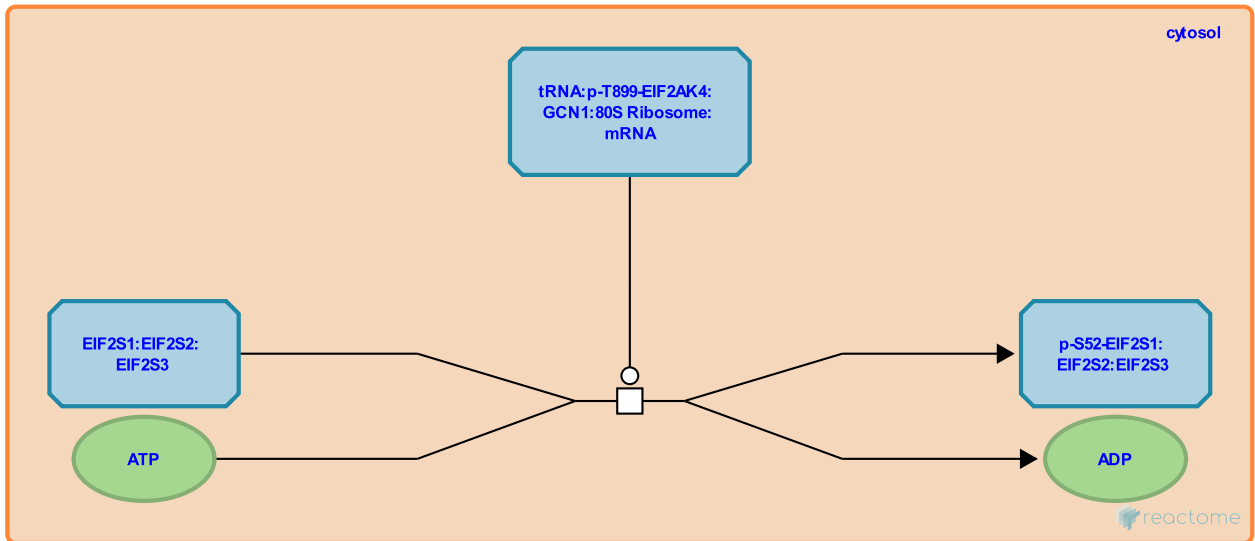
**p-T899-EIF2AK4 (GCN2) phosphorylates EIF2AS1** [↗](#)

**Stable identifier:** R-HSA-9633008

**Type:** transition

**Compartments:** cytosol

**Inferred from:** GCN2 phosphorylates SUI2 (*Saccharomyces cerevisiae*), Eif2ak4 phosphorylates Eif2s1 (*Mus musculus*)



After binding uncharged tRNA and autophosphorylating, EIF2AK4 (GCN2) phosphorylates EIF2S1 (eIF2 alpha subunit) on serine-52 (serine-51 in the rabbit homolog, inferred from mouse homologs and yeast homologs), which inhibits the guanine nucleotide exchange factor eIF2B, impairs exchange of GDP for GTP, and reduces recycling of EIF2 for initiation of translation. This causes downregulation of translation of most mRNAs, however translation of certain mRNAs possessing upstream ORFs, such as ATF4, is upregulated (inferred from mouse homologs and yeast homologs).

**Editions**

2018-12-28	Authored, Edited	May, B.
2019-09-15	Reviewed	Bruhat, A.
2019-11-20	Reviewed	Staschke, KA.