

ANG cleaves tRNA to yield tRNA halves

Basso, K., Dutta, A., May, B., Su, Z., Wilson, B.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](#). For more information see our [license](#).

03/05/2024

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: 88

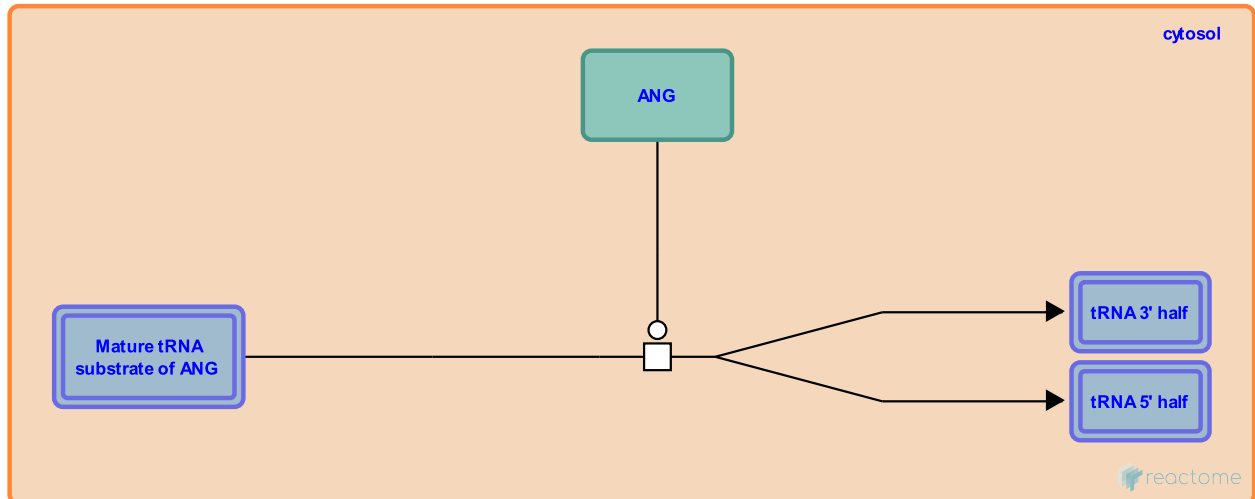
This document contains 1 reaction ([see Table of Contents](#))

ANG cleaves tRNA to yield tRNA halves ↗

Stable identifier: R-HSA-9708327

Type: transition

Compartments: cytosol



Angiogenin (ANG) cleaves within or near the anticodon of specific tRNAs including but not limited to: tRNA Arg ACG (Fu et al. 2009), tRNA Arg CCG (Fu et al. 2009), tRNA Glu CTC (Fu et al. 2009), tRNA Gly CCC (Fu et al. 2009), tRNA Gly GCC (Fu et al. 2009), tRNA Met CAT (Fu et al. 2009, Su et al. 2019), tRNA Pro AGG (Yamasaki et al. 2009), tRNA Pro TGG (Yamasaki et al. 2009), tRNA Val AAC (Fu et al. 2009), tRNA Ala AGC (Su et al. 2019), tRNA Ala CGC (Su et al. 2019), tRNA Ala TGC (Su et al. 2019), tRNA Asp GTC (Su et al. 2019), tRNA Glu TTC (Su et al. 2019), tRNA His GTG (Su et al. 2019), tRNA Leu CAG (Su et al. 2019), tRNA Leu TAG (Su et al. 2019), tRNA Lys TTT (Su et al. 2019), tRNA Ser GCT (Su et al. 2019), tRNA Ser CGA (Su et al. 2019), tRNA Val CAC (Su et al. 2019), tRNA Val TAC (Su et al. 2019) (also Lee and Vallee 1989, Saxena et al. 1992, Emara et al. 2010, Ivanov et al. 2011). The products are a 5' fragment of about 30-35 nt and a 3' fragment of about 40 nt known as tRNA halves or stress-induced tRNA fragments (tiRNAs) (Emara et al. 2010). As a result of ANG cleavage, the 5' tRNA halves contain 5' monophosphates (Emara et al. 2010) and 3' cyclic monophosphates (Shigematsu et al. 2018), while the 3' tRNA halves contain 5' hydroxyl groups (Shigematsu et al., 2018). ANG cleaves tRNA in response to biological conditions such as exposure to sex hormones and stresses such as starvation, oxidative stress, and virus infection (Fu et al. 2009, Emara et al. 2010, Ivanov et al. 2011, Wang et al. 2013, Honda et al. 2015, Selitsky et al. 2015), but several tRNA halves are still produced after stress in ANG knockout cells (Su et al. 2020). The 5' tiRNAs inhibit translation by displacing eIF4F from the m(7)G caps of mRNAs (Emara et al. 2010, Ivanov et al. 2011). The 3' tiRNAs protect cells against stress-induced apoptosis by interacting with cytochrome C (inferred from mouse homologs in Saikia et al, 2014). The products of ANG have modifications present on mature tRNAs (Drino et al. 2020); therefore, the cleavage is believed to occur in the cytosol (Yamasaki et al. 2009, reviewed in Lyons et al. 2018) perhaps as ANG is translocated from receptors on the plasma membrane through the cytosol to the nucleus.

Literature references

- Rybak, SM., Youle, RJ., Ackerman, EJ., Saxena, SK., Davey, RT. (1992). Angiogenin is a cytotoxic, tRNA-specific ribonuclease in the RNase A superfamily. *J Biol Chem*, 267, 21982-6. ↗
- Fannin, EE., Shirasaki, T., Sethupathy, P., Lemon, SM., Kaneko, S., Baran-Gale, J. et al. (2015). Small tRNA-derived RNAs are increased and more abundant than microRNAs in chronic hepatitis B and C. *Sci Rep*, 5, 7675. ↗
- Kuscu, C., Su, Z., Malik, A., Dutta, A., Shibata, E. (2019). Angiogenin generates specific stress-induced tRNA halves and is not involved in tRF-3-mediated gene silencing. *J Biol Chem*, 294, 16930-16941. ↗
- Sun, F., Zheng, X., Zhu, J., Tie, Y., Liu, Q., Xing, R. et al. (2009). Stress induces tRNA cleavage by angiogenin in mammalian cells. *FEBS Lett*, 583, 437-42. ↗
- Shigematsu, M., Rigoutsos, I., Suzuki, R., Honda, S., Imoto, I., Palazzo, JP. et al. (2015). Sex hormone-dependent tRNA halves enhance cell proliferation in breast and prostate cancers. *Proc Natl Acad Sci U S A*, 112, E3816-25. ↗

Editions

2020-11-27	Authored, Edited	May, B.
2021-02-13	Reviewed	Basso, K.
2021-02-20	Reviewed	Dutta, A., Wilson, B., Su, Z.