Butyrate Response Factor 1 (BRF1) binds and destabilizes mRNA

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

28/12/2022
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


Reactome database release: 83

This document contains 1 pathway and 6 reactions (see Table of Contents)

https://reactome.org
Butyrate Response Factor 1 (BRF1) binds and destabilizes mRNA

**Stable identifier:** R-HSA-450385

**Compartments:** cytosol

Butyrate Response Factor 1 (BRF1, ZFP36L1, not to be confused with transcription factor IIIB) binds AU-rich elements in the 3' region of mRNAs. After binding, BRF1 recruits exonucleases (XRN1 and the exosome) and decapping enzymes (DCP1a and DCP2) to hydrolyze the RNA. The ability of BRF1 to direct RNA degradation is controlled by phosphorylation of BRF1. Protein kinase B/AKT1 phosphorylates BRF1 at serines 92 and 203. Phosphorylated BRF1 can still bind RNA but is sequestered by binding 14-3-3 protein, preventing BRF1 from destabilizing RNA. BRF1 is also phosphorylated by MK2 at serines 54, 92, 203, and at an unknown site in the C-terminus. It is unknown if this particular phosphorylated form of BRF1 binds 14-3-3.

**Literature references**

Karin, M., Stoecklin, G., Ong, SE., Gherzi, R., Mann, M., Chan, EL. et al. (2001). AU binding proteins recruit the exosome to degrade ARE-containing mRNAs. *Cell*, 107, 451-64.


**Editions**

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https://reactome.org
Butyrate Response Factor 1 (BRF1) binds AU-rich element in 3' UTR of mRNA

**Location:** Butyrate Response Factor 1 (BRF1) binds and destabilizes mRNA

**Stable identifier:** R-HSA-450517

**Type:** binding

**Compartments:** cytosol

Butyrate response factor 1 (BRF1) binds AU-rich elements in the 3' untranslated region of mRNAs.

**Followed by:** BRF1 Complex recruits RNA degradation activities, MK2 phosphorylates BRF1, Protein Kinase B/Akt phosphorylates BRF1

**Literature references**


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https://reactome.org
**BRF1 Complex recruits RNA degradation activities**

**Location:** Butyrate Response Factor 1 (BRF1) binds and destabilizes mRNA

**Stable identifier:** R-HSA-450488

**Type:** binding

**Compartments:** cytosol

BRF1 recruits RNA degradation activities to hydrolyze the RNA bound to BRF1. Coimmunoprecipitation has shown BRF1 interacts with the exosome (3' to 5' nuclease), XRN1 (5' to 3' nuclease), and DCP1a and DCP2 (decapping). BRF1 localizes RNAs to processing bodies, sites of translation repression and possible sites of RNA degradation.

**Preceded by:** Butyrate Response Factor1 (BRF1) binds AU-rich element in 3' UTR of mRNA

**Literature references**

Karin, M., Stoecklin, G., Ong, SE., Gherzi, R., Mann, M., Chan, EL. et al. (2001). AU binding proteins recruit the exosome to degrade ARE-containing mRNAs. *Cell*, 107, 451-64.  

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Protein Kinase B/Akt phosphorylates BRF1

Location: Butyrate Response Factor 1 (BRF1) binds and destabilizes mRNA

Stable identifier: R-HSA-450490

Type: transition

Compartments: cytosol

BRF1 is phosphorylated at Serine92 and Serine203 by Protein kinase B/AKT. Protein kinase B is activated by phosphatidylinositol 3-kinase. Phosphorylation of BRF1 does not interfere with the ability of BRF1 to bind RNA or interact with enzymes that catalyze RNA degradation therefore larger complexes may contain phosphorylated BRF1.

Preceded by: Butyrate Response Factor1 (BRF1) binds AU-rich element in 3' UTR of mRNA

Followed by: p-S92,203-BRF1 binds 14-3-3

Literature references


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**MK2 phosphorylates BRF1**

**Location:** Butyrate Response Factor 1 (BRF1) binds and destabilizes mRNA

**Stable identifier:** R-HSA-450474

**Type:** transition

**Compartments:** cytosol

MAPK-activated protein kinase 2 (MK2) phosphorylates BRF1 at serine 54, serine 92, serine 203, and an unknown site in the C terminus. Phosphorylation inhibits the ability of BRF1 to cause degradation of RNA. It is unknown if tetraphosphorylated BRF1 binds 14-3-3 in the same way as diphosphorylated BRF1 does.

**Preceded by:** Butyrate Response Factor1 (BRF1) binds AU-rich element in 3' UTR of mRNA

**Followed by:** p-S54,92,203-BRF1 binds 14-3-3

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Phosphorylated BRF1 interacts with 14-3-3, becomes localized to the cytoskeleton, and no longer promotes RNA degradation. Phosphorylated BRF1 is, however, still able to bind RNA.

**Preceded by:** Protein Kinase B/Akt phosphorylates BRF1

**Literature references**


p-S54,92,203-BRF1 binds 14-3-3

**Location:** Butyrate Response Factor 1 (BRF1) binds and destabilizes mRNA

**Stable identifier:** R-HSA-482788

**Type:** binding

**Compartments:** cytosol

Phosphorylated BRF1 interacts with 14-3-3, becomes localized to the cytoskeleton, and no longer promotes RNA degradation. Phosphorylated BRF1 is, however, still able to bind RNA.

**Preceded by:** MK2 phosphorylates BRF1

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