

AKT phosphorylates MDM2

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28/04/2024

https://reactome.org

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)

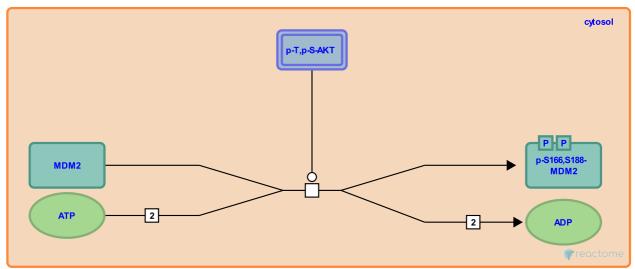
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AKT phosphorylates MDM2 对

Stable identifier: R-HSA-198599

Type: transition

Compartments: cytosol



AKT phosphorylates MDM2 on two serine residues, at positions 166 and 188 (Mayo and Donner 2001, Feng et al. 2004, Milne et al. 2004). AKT-mediated phosphorylation of the E3 ubiquitin-protein ligase MDM2 promotes nuclear localization and interferes with the interaction between MDM2 and p14-ARF, thereby decreasing p53 stability. This leads to a decreased expression of p53 target genes, such as BAX, that promote apoptosis (Zhou et al. 2001, Mayo and Donner 2001).

Literature references

Kampanis, P., Campbell, DG., Nicol, S., Milne, D., Meek, D., Fuller-Pace, F. et al. (2004). A novel site of AKT-mediated phosphorylation in the human MDM2 onco-protein. *FEBS Lett.*, 577, 270-6.

Yang, Z., Hess, D., Tamaskovic, R., Merlo, A., Feng, J., Brazil, DP. et al. (2004). Stabilization of Mdm2 via decreased ubiquitination is mediated by protein kinase B/Akt-dependent phosphorylation. *J. Biol. Chem.*, 279, 35510-7.

Mayo, LD., Donner, DB. (2001). A phosphatidylinositol 3-kinase/Akt pathway promotes translocation of Mdm2 from the cytoplasm to the nucleus. *Proc. Natl. Acad. Sci. U.S.A.*, 98, 11598-603. *对*

Zou, Y., Xia, W., Zhou, BP., Hung, MC., Spohn, B., Liao, Y. (2001). HER-2/neu induces p53 ubiquitination via Akt-mediated MDM2 phosphorylation. *Nat Cell Biol*, *3*, 973-82.

Editions

2006-10-10	Authored	Annibali, D., Nasi, S.
2007-11-08	Reviewed	Greene, LA.
2016-02-04	Reviewed	Inga, A., Zaccara, S.