

# MTOR and mTOR inhibitors

**mTOR** (mammalian target of rapamycin) is one of the important proteins of the signaling cascade. It is a serine/threonine kinase that consists of 2549 amino acids, which corresponds to 289 kDa. In mammals, this protein occurs as **mTORC1** (mTOR complex 1) and as **mTORC2** (mTOR complex 2).

## Function

For example, mTOR is used in **cell growth and cell survival**, it affects **metabolic pathways** (e.g. for insulin) and, last but not least, molecules used in signal propagation in the cell (growth factors, hormones). Functionally, it is part of the **phosphatidylinositol 3-kinase** (PI3K) family of enzymes due to its homologous C-terminus as that of PI3K. It is thus closely linked to the **PI3K-AKT** and **Ras-ERK pathways**. It regulates the translation of initiation factor 4G (or eIF4G) as well as ribosomal 40S S6 kinase (S6K1/S6K2). Disorders of this protein are thought to be associated with diabetes mellitus and various cancers. [náhled](#) | mTOR signální dráha

## mTOR inhibitors

The best-known representative is **rapamycin (sirolimus)**, which was originally administered as an immunosuppressant used after transplants, but is now indicated especially for **kidney carcinomas**. Chemically, it is a low molecular weight macrolide antibiotic produced by bacteria of the genus *Streptomyces*. Other representatives include **everolimus** and **temsirolimus**. The most common indication for the use of mTOR inhibitors is various types of cancer (that is, they serve as **cytostatics**), but the effect of these molecules on certain neurodegenerative diseases is also being intensively investigated. [náhled](#) | Sirolimus

## Mechanism of action of mTOR inhibitors

By inhibiting mTOR, the synthesis of **cyclin D** is limited (the cell is stopped in the G1 phase of the cell cycle) and **HIF-1α** (as a result, VEGF is not expressed, which would induce neoangiogenesis).

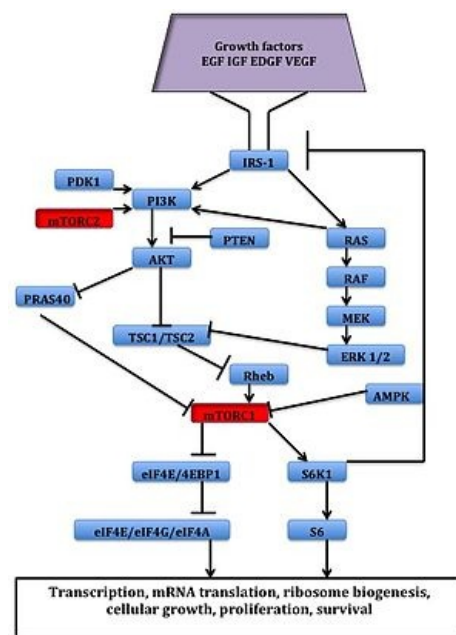
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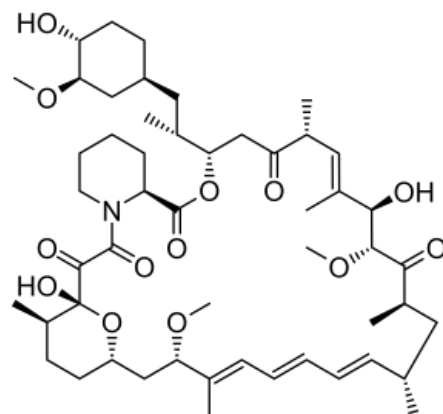
- Cytostasis
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## Resources

- JIŘINA, Martínková – AND A COLLECTIVE, . *Farmakologie : pro studenty zdravotnických oborů, 2., zcela přepracované a doplněné vydání.* - edition. Grada Publishing a.s., 2018. ISBN 978-80-271-0929-6.
- AYLETT, Christopher H. S. *Architecture of human mTOR complex 1* [online]. ©2016. [cit. 2022-02-26]. <<https://www.science.org/doi/abs/10.1126/science.aaa3870>>.
- CASTELLANOS, Mar. *Mammalian Target of Rapamycin* [online]. ©2016. [cit. 2022-02-



mTOR signaling pathway



Sirolimus

26]. <<https://www.sciencedirect.com/topics/neuroscience/mammalian-target-of-rapamycin>>.

- LAPLANTE, Mathieu. *mTOR signaling at a glance* [online]. ©2009. [cit. 2022-02-26]. <<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2758797/>>.