mTOR

The mechanistic target of rapamycin, also known as mammalian target of rapamycin (mTOR) or FK506-binding protein 12-rapamycin-associated protein 1 (FRAP1), is a protein that in humans is encoded by the MTOR gene.

MTOR is a serine threonine protein kinase that regulates cell growth, cell proliferation, cell motility, cell survival, protein synthesis, autophagy, and transcription.

mTOR belongs to the phosphatidylinositol 3-kinase-related kinase protein family. The mTOR forms two structurally and functionally distinct complexes called the mammalian target of rapamycin complex 1 (mTORC1) and the mammalian target of rapamycin complex 2 (mTORC2). mTORC1 comprises mTOR, raptor, GβL, and deptor, while mTORC2 is composed of mTOR, Rictor, GβL, PRR5, deptor, and SIN1. mTORC1 integrates signals from multiple growth factors, nutrients, and energy supply to promote cell growth when energy is sufficient and catabolism when the body is hungry. mTORC1 mainly regulates cell growth and metabolism, while mTORC2 specifically controls cell proliferation and survival [1].

Data demonstrate that mTOR signaling is significantly dysregulated in human temporal lobe epilepsy (TLE), offering new targets for pharmacologic interventions. Specifically, clinically available drugs that suppress mTORC1 without compromising mTOR2 signaling, such as rapamycin and its analogs, may represent a new group of antiepileptogenic agents in TLE patients [2].

Scholl et al., analyzed epilepsy surgery specimens of Focal Cortical Dysplasia IIB (FCD IIB) (n=22), Tuberous Sclerosis Complex (TSC) , and other malformations of cortical development MCD, and compared them to autopsy and biopsy cases. The entire lesional pathology was assessed using digital immunohistochemistry, immunofluorescence and western blotting for oligodendroglial lineage, myelin and mTOR markers, and findings were correlated to clinical parameters. White matter pathology with depleted myelin and oligodendroglia were found in 50% of FCDIIB and 62% of TSC cases. Other MCDs had either a normal content or even showed reactive oligodendrolial hyperplasia. Furthermore, myelin deficiency was associated with increased mTOR expression and the lower amount of oligodendroglia was linked with their precursor cells (PDGFRa). The relative duration of epilepsy (normalized to age) also correlated positively to mTOR activation and negatively to myelination. Decreased content of oligodendroglia and missing precursor cells indicated insufficient oligodendroglial development, probably mediated by mTOR, which may ultimately lead to severe myelin loss [3].

mTOR inhibitor

see mTOR inhibitor.

1)
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2)
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3)
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