

mTOR Part 2 of 7

mTOR is a pathway that helps controls cell growth. In the most simplest terms: When you have high mTor activation, you promote growth in the body. When you have low mTor activation, you promote repair and maintenance.

mTORC1: Raptor (associated)

Growth signals

mTORC1>S6K>Translation

mTORC2: Rictor (insensitive)

Kinase: enzyme that attaches phosphates to things

mTORC1 (Most important players)

1. mTOR enzyme

2. Raptor

Recruiting downstream targets, substrates for mTORC1

Multiple phosphorylation sites:

AMPK (catabolic enzyme) inhibits

MAPK (anabolic enzyme) promotes

Rheb promotes phosphorylation

3. MLST8 (AKA: Gable)

>Nebulin of mTOR; stabilizes the active site of mTOR

But—Also includes;

4. TSC1/2

Inhibits Rheb

5. Rheb

Promotes raptor, directly activates mTOR

Need GTP bound to Rheb to activate mTOR

6. 4EBP1

Inhibits protein synthesis

7. P70S6K (kinase=phosphorylating)

8. RpS6

Protein synthesis

9. Deptor (inhibitor)

Inhibits kinase (phosphorylation)

Halts apoptosis

>Increase in mTOR, suppressed Deptor expression

10. PRAS40 (inhibitor)

Inhibition of the mTOR enzyme via FKBP12

>Inhibits S6K1's phosphorylation of RpS6

mTORC2 regulates: protein translation, organization of actin cytoskeletons, ion transport and metabolism

>Phosphorylates PKB, SGK and PKCa

>SGK1 regulates ion and solute transport

>mSin1 recruits SGK1 to the mTOR complex to be phosphorylated

>Protor-1 recruits SGK1 to the mTOR complex

Linking complex 2 to complex 1

>AKT/PKB, inhibits TSC1/2 (hydrolyzes GPD)

The mTOR Relay Race:

- PI3K (phosphatidylinositol 3 kinase) gets activated by something

- This phosphorylates PIP2 to PIP3

- PIP3 docks PKB where it is phosphorylated (activated) by PDK (inhibits the TSC)

- TSC1/2 (2 is tuberlin) normally turns off Rheb by hydrolyzing it's GTP.

- Rheb-GTB binds to mTOR and activates

- mTORC1 phosphorylates p70s6k, 4e-bp1 and eIF4G

- p70s6k phosphorylation positively regulates rps6, that leads to the translation of mRNAs, increasing translation capacity

- When 4e-BP1 is phosphorylated, it is deactivated, which leads to increased RATES of translation initiation, increasing translation efficiency

- Translation: ribosomes synthesize protein using mRNA transcript

- Result: Hypertrophy (as a result of translational capacity AND efficiency)