

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)