

mTOR Part 5 of 7

AMPK: Metabolic Dictator

As metabolic enzymes increase, so does VO₂ Max

Enzymes that enhance endurance metabolism:

- Mitochondrial enzymes
- Glycolytic enzymes
- Fatty Acid metabolism

AMPK: Helps regulate the energy status of your muscle during endurance sports, and prevents mTORC1 from phosphorylating tuberlin and raptor

How does AMPK accumulate?

- Exercise
- Hypoxia
- Starvation/glucose deprivation

ATP Hydrolysis;

Building up a bunch of ADP and losing ATP

- Adenylate kinase
- AMP binds to beta unit on AMPK .. When ATP binds; it inhibits

Your AMP can be deaminated to form inosine monophosphate (IMP) and ammonia (NH₃)

*No longer interacting with AMPK

AMPK has two regulatory: Beta and Gamma

Gamma is where AMP binds

High levels of AMP activate AMPK by 3 different mechanisms:

1. Direct allosteric activation of its kinase activity
2. Increasing activation loop by phosphorylation by upstream kinase
3. Protection of the phosphorylated activation loop against dephosphorylation

Part of AMPK's role is to take up carbs (GLUT4 translocation), so its helpful to sense carb levels within the cells as a component of total stored and available cellular energy

-GLUT4 binds with Beta subunit

Recap:

1. ATP hydrolysis: $ATP + H_2O \rightarrow ADP + P_i + H^+$
2. Adenylate kinase reaction: $ADP + ADP \rightarrow ATP + AMP$
3. ATP and AMP compete for binding on gamma subunits on AMPK; ATP inhibits alpha phosphorylation; AMP promotes it
4. Binding of first AMP on gamma enhances binding of a second
5. With two AMPs bound, an upstream kinase (LKB1) activates AMPK by phosphorylating the alpha subunit

AMPK and mTOR regulate autophagy through direct phosphorylation of UP

Metformin activates AMP kinase through inhibition of AMP Deaminase

-Diabetes