

MUSCLE PHYSIOLOGY LECTURE 29

mTOR - mammalian target of rapamycin

mTOR is this critical regulator of skeletal muscle metabolism, anabolic cell growth and proliferation. Interaction can accelerate/permit growth response to exercise. Everyone can do it, even if people are genetically different. People who have a head start won't necessarily end up first.

Differences between mTOR complex 1 and mTOR complex 2

mTOR complex 1 and mTOR complex 2 are independently regulated by distinct binding partners. mTORC1 contains RAPTOR and PRAS40, while mTORC2 contains RICTOR, MSIN1, and PROTOR. mTORC1 controls cell growth by regulating protein synthesis via phosphorylation of its downstream substrates. mTORC2 regulates cell proliferation, survival, and the actin cytoskeleton by activating AKT, p70S6K, and SGK-1.

mTORC1 - mTOR enzyme, RAPTOR (regulatory associated protein of target of rapamycin), MLST8 (mammalian lethal with SEC13 proteins)

mTORC2 - mTOR enzyme, RICTOR (rapamycin-insensitive companion of target of rapamycin), MLST8 (mammalian lethal with SEC13 proteins)

MSIN1 (mammalian stress-activated protein kinase interacting protein 1)

mTORC1 - most critical regulator of skeletal muscle metabolism (protein synthesis and degradation) mTORC2 - promoting stress responses needed for cell survival. RAPTOR functions as a scaffolding protein that facilitates the recruitment of substrates to the mTOR kinase.

multiple RAPTOR phosphorylation sites - can be activated or inhibited by phosphorylation. Rheb promotes RAPTOR phosphorylation positively.

site-specific RAPTOR phosphorylation by AMPK, RSK, and mTOR modulates mTORC1 activity either positively or negatively.

deTOR - inhibitory protein that is phosphorylated by mTORC1, receiving it of its inhibitory effects. PRAS40 - inhibitory protein promoting more and efficient translation is hypertrophy.