Introduction to LaTeX

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Abstract

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1 Introduction

- Time course of pS6K in AA and AA + rapamycin conditions [1]
- Rheb activates AMPK and reduces p27 in TSC2 null cells which in turn reduces cdk2 [2]
- Rheb is constitutively active in TSC2 knockout cells [2]
- In TSC2 null cells, down regulating Rheb down regulated mTORC1 and s6k
- TSC2 is a GAP for Rheb [**?**]
- The more TSC2 in the system the more Rheb that is hydrolysed [3]
- Rheb-GTP is an activator of mTORC1, measured by an increase in S6K and 4EBP phos
- The more RhebGTP present the more mTORC1 activation and S6K/4EBP phos [3]

1.1 [**?**]

- mTORC1 phosphorylates Akt at S473

1.2 [**?**]

This is a review

- Amino acids inhibit TSC2

1.3 [?]

- Insulin and amino acids both stimulate mTORC1 individually and synergize together
- Wortmannin inhibits these reactions

1.4 [?]

AMPK and energy review

- During muscle contraction, glucose is used to generate ATP. AMPK enhances this process
- Muscle glucose uptake is also promoted by insulin, when the fate of glucose is storage as glycogen
- GLUT4 mediates the glucose update in both of these situations
- GLUT4 are glucose transporters that reside in vesicles near the plasma membrane
- GLUT4 containing vesicles need to fuse with the plasma membrane to allow them to transport glucose
- This fusion requiers RAB G proteins in their GTP bound state, though RAB G proteins are basally exist in their GDP bound state
- RAB G proteins are held in an inactive GDP bound state by RAB-GAP proteins, one of which is called Akt substrate 160 (AS160 / TBC1D4) and TBC1D1, both of which are associated with the GLUT4 containing vesicles
- Akt phos AS160 in muscle and adipocytes allowing it to associate with 14-3-3 proteins which leads to disociation from the vesicles
- AMPK also phosphorylates TBC1D1 in contracting muscle, also recruits 14-3-3 prroteins and leading to dissociation from vesicles
- In both biological contexts, the Rab-GAP dissociation results in the loading of Rab with GTP and fusion of GLUT4 containing vesicles with the membrane
- .

1.5 [?]

- GREB1 gene response to E2 treatment via the estrogen receptor
- GREB1 is required for hormone dependent proliferation
- knock down of GREB1 results in growth arrent

- overexpression of GREB1 results in oncogenic senescence
- GREB1 regulates PI3K/Akt/mTORC1
- Growth arrested BC cells from GREB1 knock down can be rescued by constitutive Akt activation

1.6 [?]

- A mechanism of resistance to endocrine therapies is overexpression of HER2
- but only a small portion (around 10%))

1.7 [?]

-

1.8 [?]

-

1.9 [?]

-

1.10 [?]

- RAG proteins bind TSC2.
- Therefore, RAGs not only activate mTORC1 by inducing their recruitment to the lysosome under AA stimulation, they also actively actively repress mTORC1 in the absence of AA
- binding between rag proteins and TSC2 increases upon AA removal
- TSC2 is recruited to lysome in a Rag dependent manner when AAs are removed
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  - TSC is cytoplasmic when AA present
  - On removal TSC2 quickly accumulates on lysosomal surface (15 min)
  - impaired Rag protein integrity blunts lysosomal accumulation of TSC2 upon AA removal and reduced mtorc activation on AA readdition
- TSC2 is required for complete inactivation of mTORC1 when AAs are removed
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  - cells lacking TSC2are unable to completly inactivate mtor on AA removal

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