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Does REDD1 act as an AMPK-like in skeletal muscle ?

Florian A. Britto¹, Yassine Belloum¹, Christelle Ramonatxo¹, Elodie Jublanc¹, Fabienne Cortade¹, Béatrice Chabi¹, Damien Freyssenet², Sophie Giorgetti-Peraldi³, Vincent Ollendorff¹, François B. Favier¹

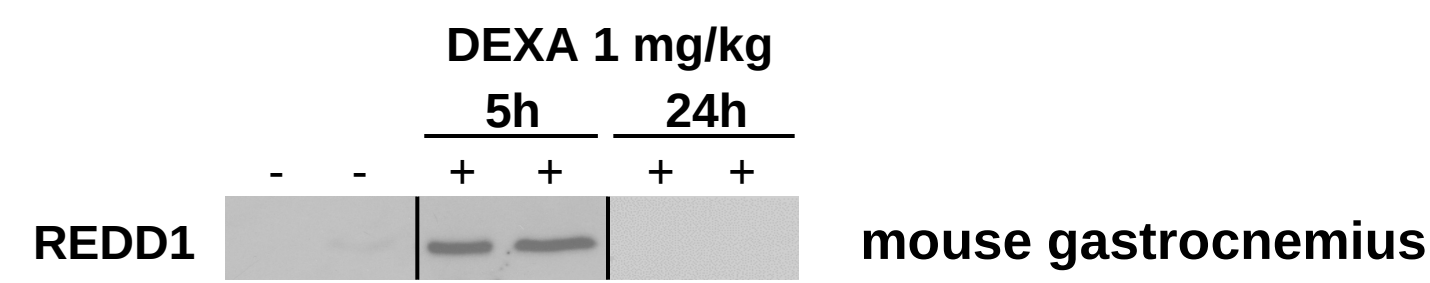
¹UMR INRA 866 Dynamique Musculaire & Métabolisme, Université de Montpellier, Montpellier, France

²Laboratoire Interuniversitaire de Biologie de la Motricité, EA 4338, Université de Lyon, Université Jean Monnet, Saint Etienne, France

³INSERM 1065, Mediterranean Research Centre for Molecular Medicine, Nice, France

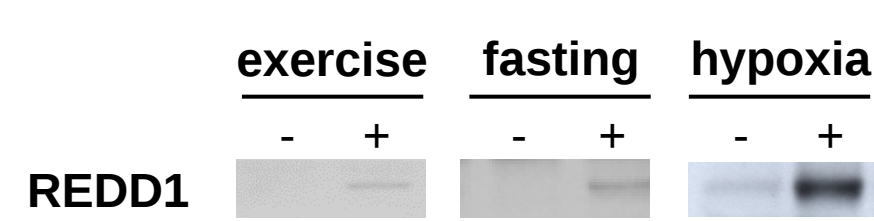
REDD1 is a stress response protein

REDD1 induction by glucocorticoids

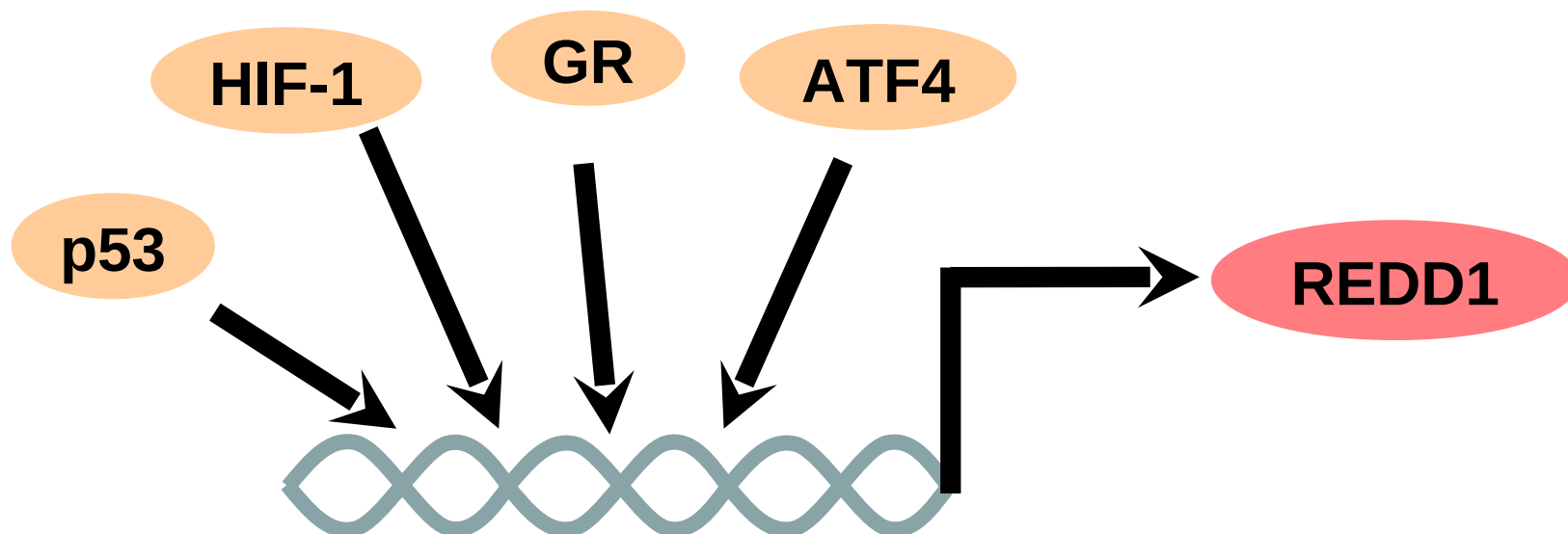


- Low basal expression
- Short half-life

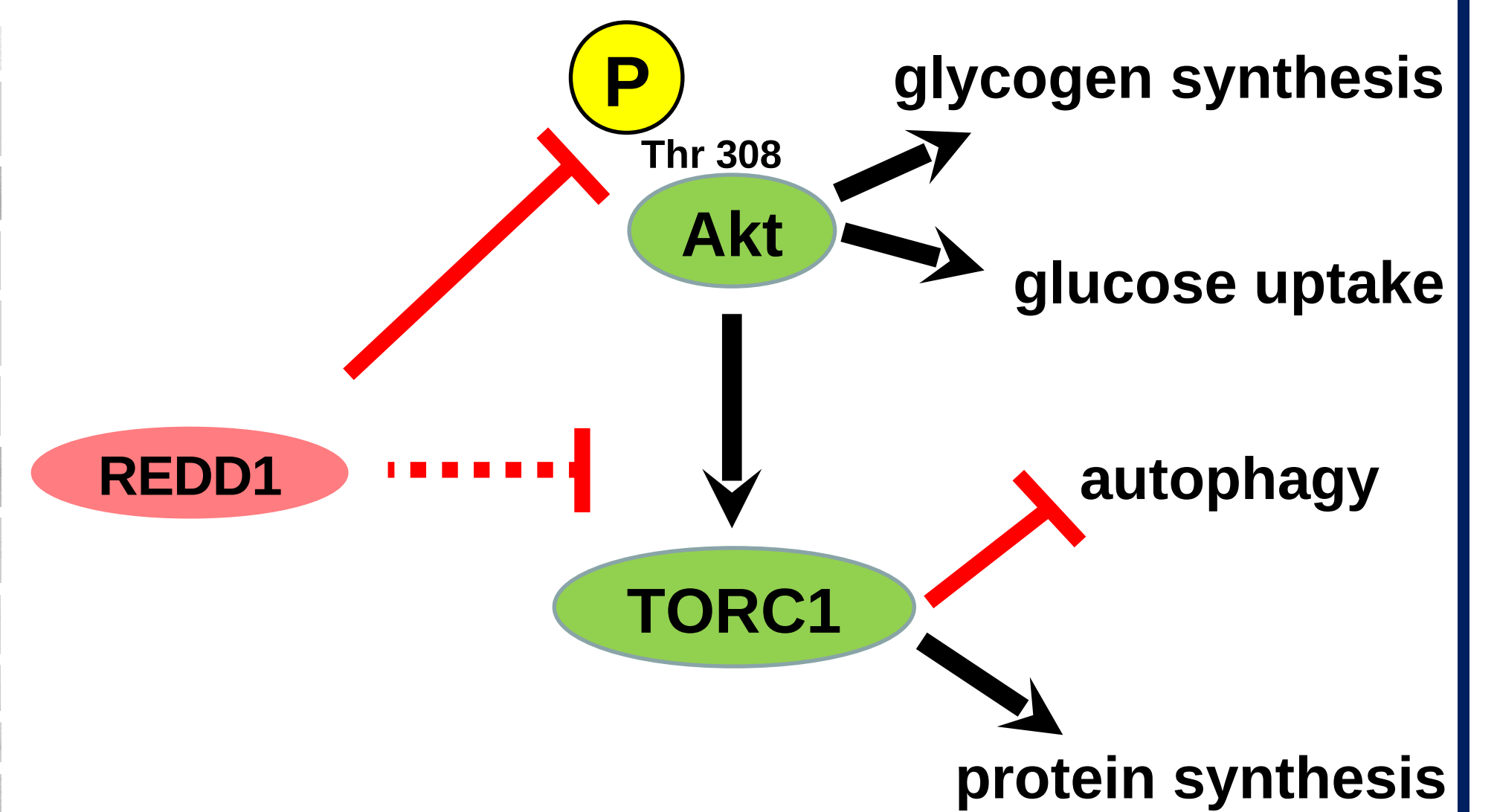
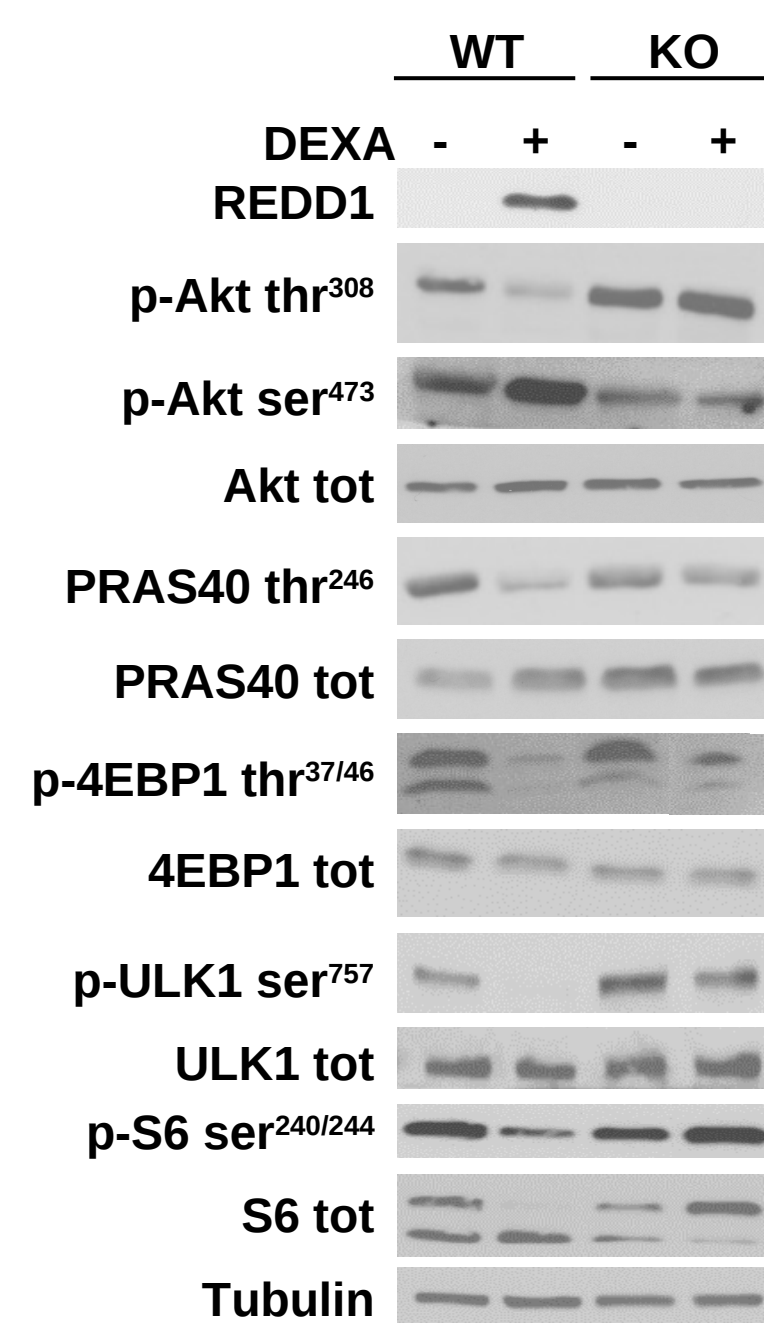
- 90-min running exercise (mouse gastrocnemius)
- 16-h fast (mouse gastrocnemius)
- 3 wk of hypobaric hypoxia (6,000 m, rat soleus)



- REDD1 induction in response to metabolic challenge



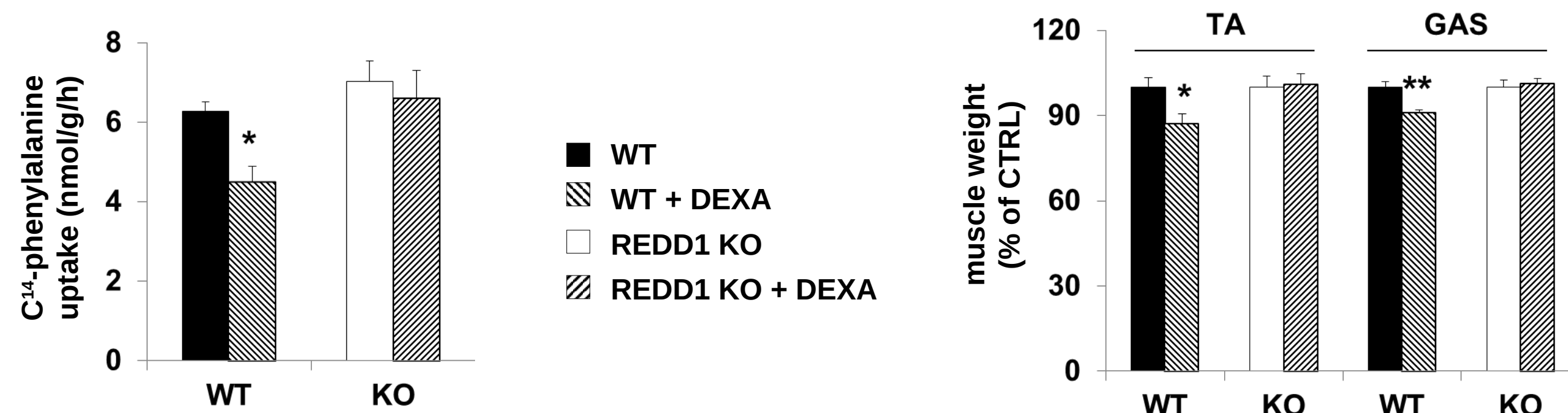
REDD1 inhibits Akt/TORC1



- The deletion of REDD1 impedes the inhibition of the Akt/TORC1 pathway in response to dexamethasone (mouse gastrocnemius)

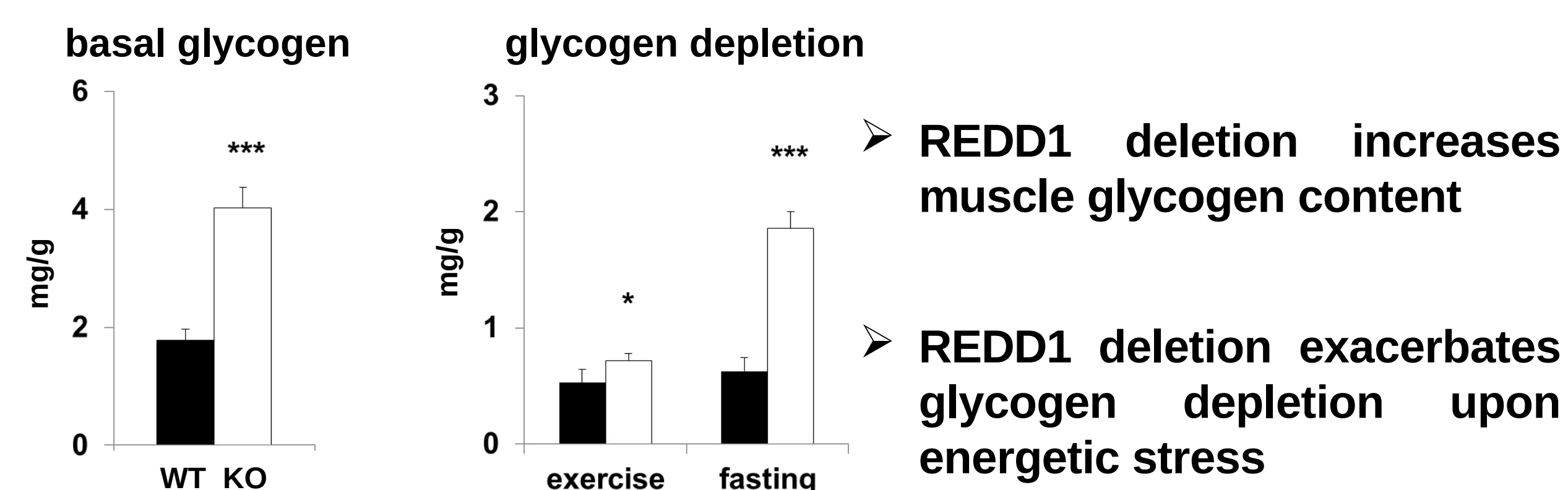
REDD1 alters nutrients storage

Protein synthesis & muscle mass



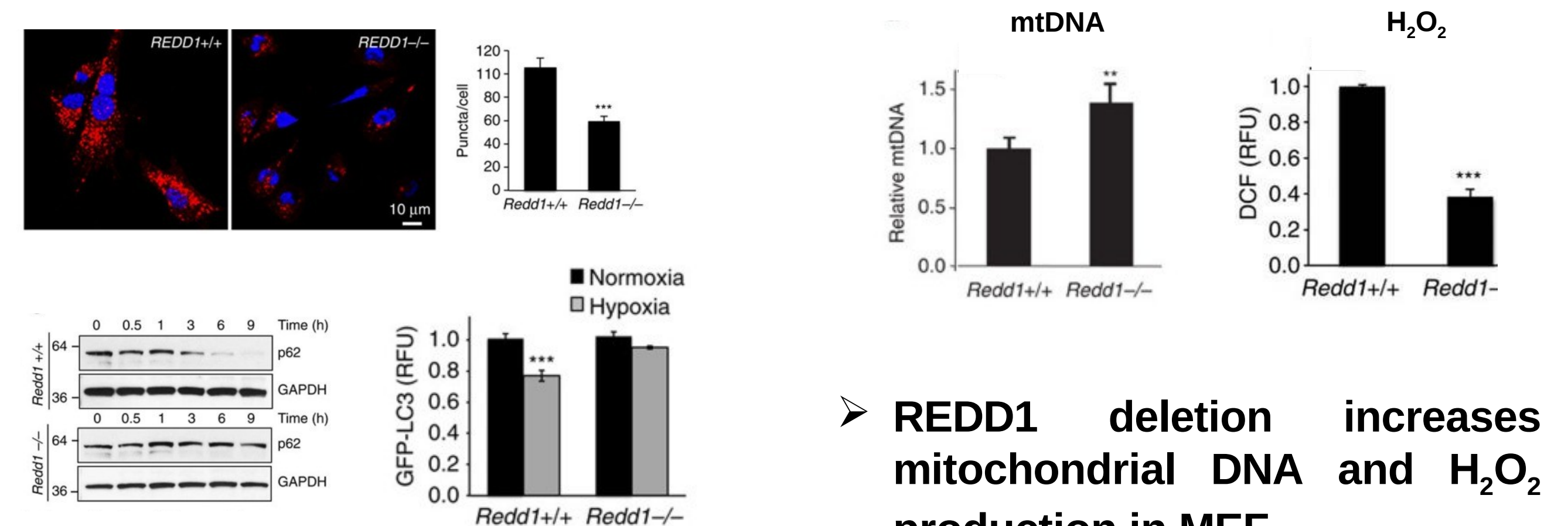
- REDD1 deletion abolishes the decrease in protein synthesis and in muscle mass after dexamethasone administration (mouse gastrocnemius)

Glycogen stores



- REDD1 deletion increases muscle glycogen content
- REDD1 deletion exacerbates glycogen depletion upon energetic stress

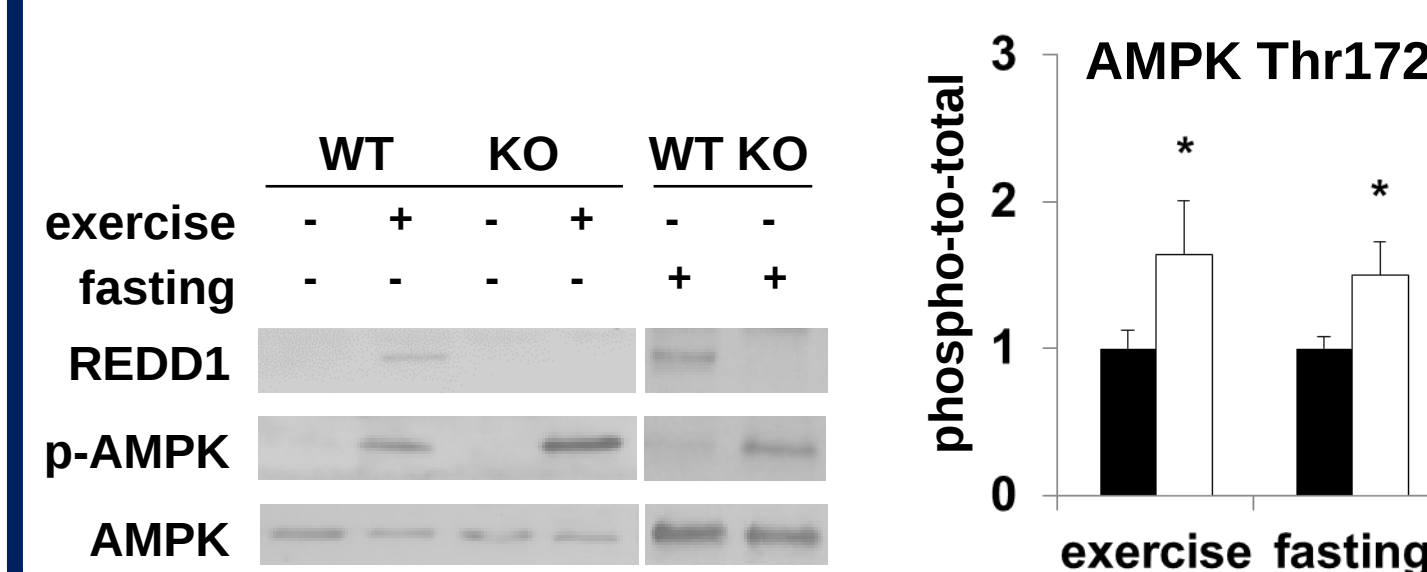
REDD1 promotes mitophagy



- Basal and hypoxia-induced ATG are reduced in REDD1^{-/-} MEF

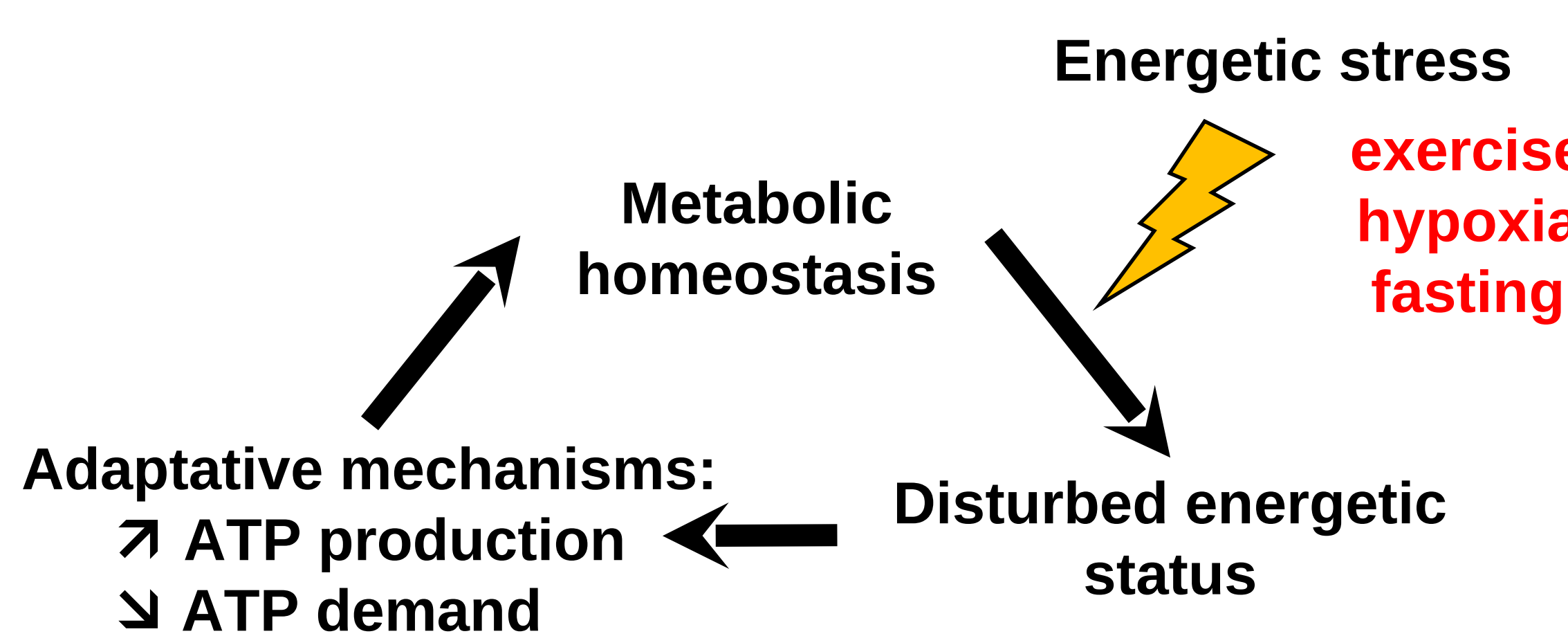
Qiao et al., 2015 Nat Commun

AMPK activation is related to REDD1 upregulation

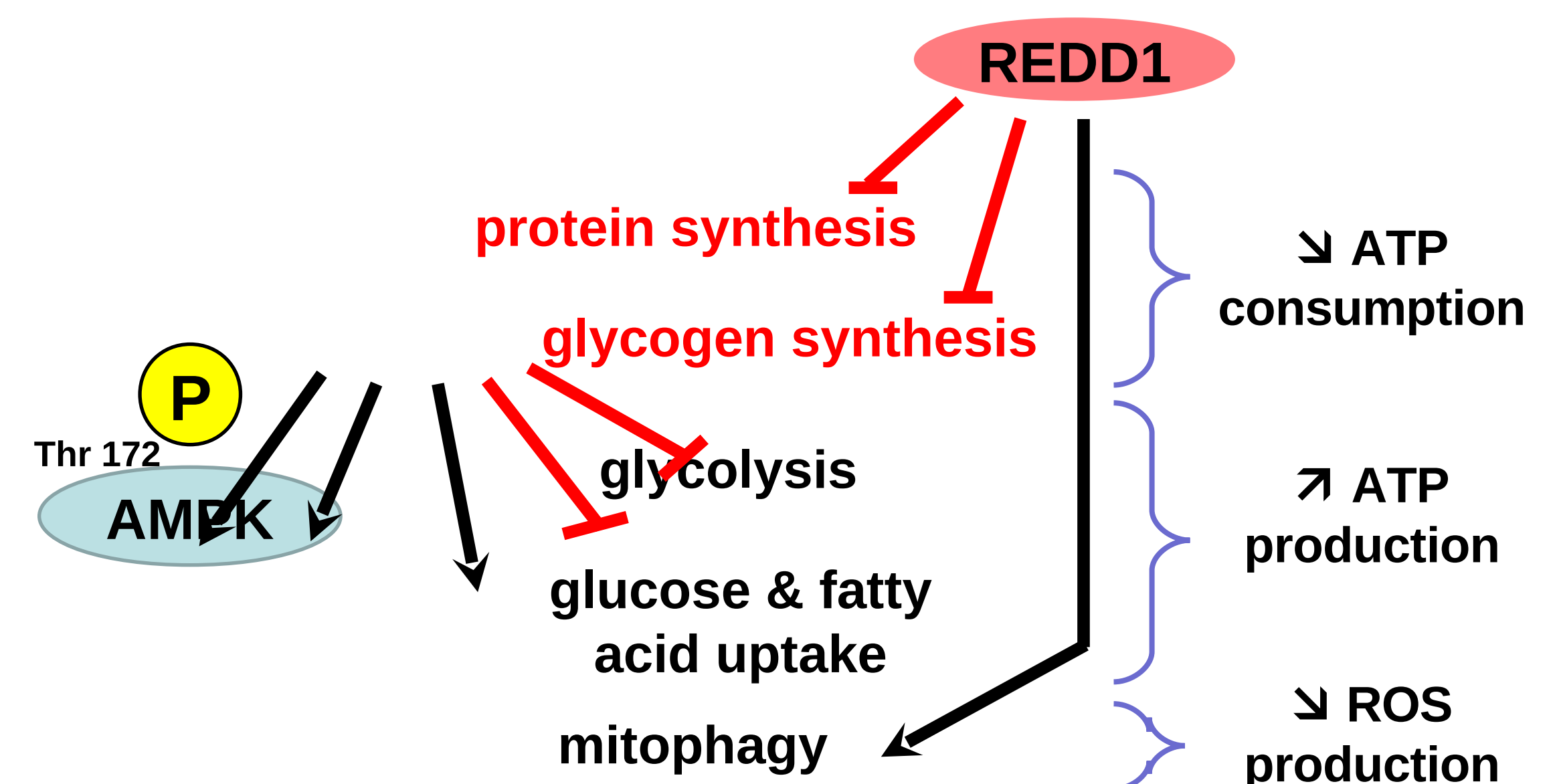


- AMPK activation is exacerbated in REDD1 KO mice upon energetic stress

Conclusion



- By slowing down anabolic processes, REDD1 would spare ATP and delay AMPK activation



References

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➤ Qiao et al., 2015 *Nat Commun.* 2015 Apr 28; 6: 7014.

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