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ÍNDICE RESUMIDO:

MR3.3. TOR BIOLOGY IN *ECHINOCOCCUS* sp.: ITS ROLES IN THE CELLULAR COORDINATION OF MULTIPLE METABOLIC AND TRAFFICKING PATHWAYS… HUGE AND POWERFUL AS THOR.

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Evolutionary conserved insulin/TOR pathway is an essential network of outputs and effectors for the development of *Echinococcus* larval stage. Molecular and biochemical assays, allowed us to corroborate the parasite-derived insulin receptors and host´s insulin interaction. The insulin signaling regulates anabolic functions in metacestodes and protoscoleces, suggesting the insulin/TORC1 activation. Insulin treatment activates downstream signaling components, such as phosphorylation of parasite AKT and TOR, which leads to nutrients uptake, overexpression of glucose transporters, induction of mitochondrial metabolism, and lipid droplet and glycogen synthesis stimulation, both crucial reserve molecules in this cestode. Similar to its orthologs, *Echinococcus*-TOR is a high-molecular-weight protein that contains all preserved structural domains, with two conserved insulin-dependent phosphorylation hot spots (Thr^{3119}- Ser^{3122}) likewise to vertebrate. However, *Echinococcus*-TOR, possess an additional peptide with coil structure into regulatory domain, similarly others parasite helminths, with potential druggability and specificity for TOR kinase. Furthermore, we analyzed in which manner the inactivation of TORC1 induces autophagy and arrests the parasites survival. Indirect inhibition of TORC1 in presence of metformin, causes an increase in autophagy genes transcription, through overexpression and activation of transcription factor EB (TFEB), whose phospho-activation and nuclear translocation is TORC1-dependent. TFEB is a master regulator that controls essential processes in the life cycle of *Echinococcus* sp. as the endo-exocytosis (necessary in absence of digestive/excretory systems) and the biogenesis of autophagy key organelles as autophagosomes and lysosomes (given conditions of constant nutrient deficiency). Lastly, based on electron microscopy data, we showed that TFEB may induce ER-phagy in metformin-treated parasites, previous identification of ER specific receptors.

Echinococcus; INSULIN; TOR; TFEB, AUTOPHAGY.

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