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Role of FoxO in the regulation of Metformin-stimulated energy stress in *Echinococcus spp*

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We have previously shown that Metformin (Met), an anti-hyperglycemic and anti-proliferative drug, exhibits considerable in vitro and in vivo activity against *E. granulosus* metacestodes. Here, we extended the study and demonstrated that the drug also possess chemopreventive properties against alveolar echinococcosis in mice. As drug administration was shown to induce the Eg-AMPK activation, its anti-echinococcal effects might be a consequence of cellular energy charge depletion in the parasite. Based on this and the fact that only one FoxO transcription factor is present in the genome of *Echinococcus spp,* the aim of this work is investigate the activation state of FoxO and its relation with the expression of genes encoding sirtuins and key autophagy-related proteins in parasites incubated under both control and energy-stress conditions. Eg-FoxO sequence reveals several post-translationally modifiable residues highly conserved. By in totoimmunolocalization assays, we detected the expression and subcellular localization of a phosphorylated (Ser352) and an acetylated (Lys373) form of Eg-FoxO in control and Met-treated protoscoleces. Interestingly, similar expression patterns were observed in both samples. Additionally, by qPCR analysis, we found that Met produced an increase in the transcriptional expression of sirt and/or atg genes in *E. granulosus* protoscoleces and metacestodes and in *E. multilocularis* primary cells. In this regards, BLASTn analysis of the upstream sequences in putative promoters of several of these genes showed the conserved binding motif described for FoxO-activated genes. These results suggest a possible role of FoxO in the transcriptional regulation of *Echinococcus spp*. under energy stress conditions. We also detected expression of Atg8 polypeptide (LC3) with both a diffuse and punctate staining in control and Met-treated *E. granulosus* protoscoleces and *E. multilocularis* vesicles. However, western blot analysis demonstrated higher levels of Eg-Atg8-PE (LC3-II) in Met-treated protoscoleces, suggesting a possible induction of autophagy under this condition. Altogether, our data indicate that FoxO, Sirt and autophagy might participate in the regulation of Met-stimulated energy stress in *Echinococcus spp*.

Biography

Julia A Loos has a PhD in Biological Science (National University of Mar del Plata, 2017) and she is currently working as a postdoc under the direction of Prof. Dr. Andrea Cumino. She has been serving as assistant teacher for subjects such as Histology, General Microbiology and Pharmacology that are part of the Biology, Biochemistry and Medicine courses of study. She participates in several research projects on Parasitology and has published original articles. Currently, her research is focused on the study of intermediary metabolism and energy control in the larval stage of *Echinococcus spp*.

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