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Cordycepin induced unfolded protein response-dependent cell death with drug resistance phenomenon in MA-10 mouse testicular cancer cells

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Testicular cancer is the most commonly diagnosed cancer in men at 15-35 years of age, and radical orchidectomy combined with chemotherapy is the typical treatment. However, drugs resistance and side effects that impact quality of life for patients with testicular cancer has not seen marked improvement in recent decades. In the present study, we characterized the pharmacological exacerbation of the unfolded protein response (UPR), which is an effective approach to kill testicular cancer cells. The UPR is executed via distinct signaling cascades whereby endoplasmic reticulum (ER) during stress is complemented by an apoptotic response if the defect cannot be resolved. To characterize the ability of cordycepin (3'-deoxyadenosine), a major bioactive component in *Cordyceps sinensis* with anti-tumor ability, inducing ER stress in testicular tumor cells, we have engineered a clustering analysis of mRNA expression profiles and the immunoblotting examination after cordycepin-treated MA-10 cells. Cordycepin effectively induced cell cycle arrest in MA-10 cells, and regulated FoxO/P15/P27/CDK4 signaling pathways. As well, cordycepin induced PERK/eIF2 α /ATF3/CHOP (apoptotic) and the IRE1/XBP1 (adaptive) UPR pathways. Interestingly, cordycepin-treated MA-10 cells were collected from attachment and suspension portions and then re-cultured for 72 hours, and AKT, LC3 I/II and MAPK signaling pathways were highly induced in attachment cells, illustrating the drug-resistance to cordycepin by activating AKT and MAPK pathways in MA-10 cells. In summary, PERK/eIF2 α /ATF3/CHOP signaling is required for pro-apoptotic UPR in MA-10 cell death following cordycepin treatment, suggesting a potential therapeutic application in treating testicular cancer. However, activation of AKT and MAPK pathways could possibly result in drug-resistance to cordycepin in MA-10 cells.

Biography

Bu-Miin Huang is the full time Professor at the National Cheng Kung University under the discipline Anatomy, Histology, Cell Biology, Neuroanatomy. His major interest has been focused on the *in-vitro* and *in-vivo* regulation of steroidogenesis in male and female reproductive systems by different factors such as Chinese herbs, neuropeptides, drugs and environmental toxicants.

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