

same conditions. GST protein didn't bind with target mRNAs and didn't affect proteasome cleavage activity.

Conclusion: HuR protects c-fos mRNA from proteasome ribonuclease cleavage in vitro, but can't prevent c-myc mRNA degradation. HuR and proteasome compete with each other for manifestation of their opposite activities. Thus, a new mechanism of regulation of proto-oncogenes expression was observed. However, the functional role of this process in vivo should be evaluated in further studies.^{1–4}

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PS156

Metformin interferes with glucose cellular uptake by both estrogen and progesterone receptor-positive (MCF-7) and triple-negative (MDA-MB-231) breast cancer cell lines



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Aim: Transport experiments with 3H-DG, culture growth and proliferation rate assays were performed. This work aimed to investigate the possible interference of metformin with glucose uptake by MCF-7 and MDA-MB-231 human breast adenocarcinoma cell lines as a mechanism contributing to its anticarcinogenic effect.

Introduction: Breast cancer, the most common cancer among women, remains one of the leading causes of mortality among women worldwide.¹ Metformin has been widely used as a treatment for type 2 diabetes for over 40 years.² The first report of a reduced risk of developing cancer for diabetic patients treated with metformin was published in 2005.³ Several mechanisms of action of metformin appear to be implicated in this effect.^{2,4}

Methods: Transport experiments with 3H-DG, culture growth and proliferation rate assays were performed.

Results: Acute (26 min) exposure of MCF-7 cells to metformin significantly inhibited uptake of 3H-deoxy-D-glucose (3H-DG) (maximal inhibition found with metformin 0.5 mM: 27 ± 2% reduction). Chronically (24 h), metformin induced a concentration-dependent increase in 3H-DG uptake (maximal increase observed with metformin 1 mM: 81 ± 15% increase). Acute (26 min) exposure of MDA-MB-231 cells to metformin slightly inhibited uptake of 3H-DG (maximal inhibition found with metformin 1 mM: 10 ± 3% reduction). Chronic (24 h) exposure to metformin significantly increased 3H-DG uptake by MDA-MB-231 cells (maximal increase observed with metformin 1 mM: 30 ± 8% increase).

Chronic (24 h) exposure of both cell lines to metformin (1 mM) decreased culture growth/cell mass; in contrast, it increased cell proliferation rates. Combination of metformin (1 mM) with the facilitative glucose transporter (GLUT) inhibitor kaempferol (30 μM) did not result in a more marked effect on culture growth and cell proliferation rates.

Conclusion: Summarizing, chronic exposure of MCF-7 and MDA-MB-231 cells to metformin induces a marked increase in glucose uptake, associated with an anticarcinogenic effect of the drug. We suggest that the increase in glucose uptake is a compensatory mechanism to cellular energy depletion induced by metformin.

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PS162

Endocannabinoids induce placental trophoblast reticulum stress



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Aim: We aim to investigate in cytotrophoblasts whether these effects on cell viability loss are due to endoplasmic reticulum (ER) stress mediated apoptosis.

Introduction: Placental development relies on a balance between proliferation, differentiation and apoptosis of trophoblasts, a process tightly regulated by growth factors, cytokines and hormones. Endocannabinoids (eCB), such as 2-arachidonoylglycerol (2-AG) and anandamide (AEA) may play a role in these processes. We previously demonstrated that both eCB induced trophoblast cell death.^{1,2} Here we investigated in cytotrophoblasts whether these effects on cell viability loss are due to endoplasmic reticulum (ER) stress mediated apoptosis.

ER stress is caused by the accumulation of unfolded proteins leading to an unfold protein response (UPR) triggered by transmembrane ER signaling proteins including: pancreatic ER kinase (PKR)-like ER kinase (PERK), inositol-requiring enzyme 1 (Ire1) and Activating transcription factor 6 (ATF6). The dissociation of Grp78 (BiP) from these sensors triggers a series of mechanisms that can restore homeostasis or lead to apoptosis. Placental stress has been implicated in the pathophysiology of pregnancy complications, including growth restriction and pre-eclampsia.

Methods: BeWo cells (ATCC, USA), an accepted model of cytotrophoblast stem cells were treated with AEA or 2-AG (10 micromolar) for 24 h. Through quantitative real time polymerase chain reaction (qPCR), we evaluated mRNA levels of ER stress markers: CHOP, Grp78, ATF4 and spliced mXBP1. Protein expression of CHOP was evaluated by western-blot.

Results: After 24 h of treatment with both eCB, we found an increase in mRNA levels of ER stress markers: CHOP, Grp78, ATF4 and spliced mXBP1. Protein expression of CHOP also increased in both cases.