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In Cervical Cancer Cells, Increased O-Glcnacylation Enhances the IGF-1 Receptor/Phosphatidyi Inositol-3 Kinase/Akt Pathway

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Commentary

Cervical squamous cell carcinoma (CSCC) is a kind of cancer that affects millions of women and their families around the world. CSCC is caused by the human papillomavirus (HPV), and squamous intraepithelial lesions (SILs) caused by high-risk HPV (HR-HPV) infection are considered precancerous lesions. In a prior study, HPV-infected cancer cells were able to survive by combating lipid peroxidation. According to recent study, ferroptosis kills cancer cells by an iron-dependent lipid peroxidation mechanism, and it has been recommended as a potential method for female cancer therapy [1]. The role of ferroptosis in SIL progression into CSCC was examined in this study. Ferroptosis was detected in SIL, but anti-ferroptosis was reported in CSCC. Our findings also revealed that persistent ferroptosis resulted in an antiferroptotic impact, which aided oncogenesis. Overall, we offer new insight into the role of ferroptosis in the formation of cervical SIL and identify a potential therapeutic target for the therapy of CSCC [2].

Undernutrient stress, the basic mechanisms of methionine adenosyltransferase 2 A (MAT2A)-mediated cervical cancer growth remain mostly unknown. As a result, the goal of our research is to learn more about the molecular mechanisms behind MAT2A-induced cervical oncogenesis. Immunoprecipitation, immunoblotting, and mass spectrometric analysis were used to investigate the interaction between MAT2A and programmed cell death protein 6 (PDCD6) in cervical cancer cell lines. Immunoblotting was used to detect associated pathways using a panel of inhibitors linked to stress responsive kinases. CCK-8 and flow cytometry were used to examine cell growth and apoptosis [3]. In cells with the PDCD6 K90 methylation mutation, the levels of apoptosis-related proteins Bcl-2, Bax, and Caspase-3 were also examined. T Immunohistochemistry was used to detect a link between MAT2A and PDCD6, and clinicopathological features were examined further. We discovered that AMPK activation mediates the interaction between MAT2A and PDCD6, which facilitates PDCD6 K90 methylation and further promotes PDCD6 protein stability. PDCD6 K90R expression causes an increase in apoptosis, which limits the development of cervical cancer cells when glucose is depleted. Furthermore, the clinical study shows that the MAT2A protein level is positively related to the PDCD6 level, and that a high PDCD6 level is associated with a bad prognosis and advanced stages of cervical cancer patients. We conclude that MAT2A promotes cervical cancer growth by facilitating PDCD6 methylation during glucose deprivation, implying a regulatory role for MAT2A in cellular response to nutritional stress and cervical cancer progression [4].

O-GlcNAcylation (O-GlcNAcylation) is a reversible post-translational modification that occurs on serine and threonine residues in cytosolic, nuclear, and mitochondrial proteins. OGT (O-GlcNAc transferase), which adds GlcNAc to proteins, and OGA (O-GlcNAcase), which removes it, control the level of O-GlcNAcylation. Many cancer cell types, including cervical cancer cells, have abnormal levels of protein O-GlcNAcylation. The effect of increasing protein O-GlcNAcylation on CaSki cells originating from cervical carcinoma was investigated in this work. Thiamet G (an inhibitor of OGA) and glucosamine (which gives UDP-GlcNAc substrate to OGT) pharmacologically enhanced protein O-GlcNAcylation increased CaSki cell proliferation, migration, and survival [5]. Furthermore, we discovered that enhanced O-GlcNAcylation enhances autophosphorylation of the IGF-1 receptor (IGF1R), perhaps via inhibiting the activity of protein tyrosine-phosphatase 1B. In CaSki cells, this was linked to enhanced IGF-1-induced phosphatidyl-Inositol 3-phosphate synthesis at the plasma membrane as well as increased Akt activation. Finally, we found that the levels of protein O-GlcNAcylation and Akt phosphorylation were higher in human cervical cancer samples than in healthy cervix tissues, and that there was a strong link between O-GlcNAcylation and Akt phosphorylation in these tissues. Our findings suggest that enhanced O-GlcNAcylation may play a role in cervical cancer cell growth and proliferation via stimulating IGF1R/Phosphatidyl inositol 3-Kinase (PI-3K)/Akt signalling [6].

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