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News & Comments

Metformin, an Anticancer Agent on Oral Cancer Cells

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Oral cancer (OC) is one of the most common cancer-related causes of mortality on the planet. OSCC (Oral Squamous Cell Carcinoma) is the most frequent kind of OC, accounting for 91% of all OC cases. The OSCC is responsible for 1-2% of all human cancers. The current treatment for OC is surgical resection in conjunction with or without radiation or chemotherapy. Metformin, an oral biguanide drug mostly used to treat type 2 diabetes, has shown anticancer activity against several malignancies. Metformin is being tested in clinical trials to treat a variety of cancers. Metformin has also been linked to better clinical outcomes in people with OSCC. However, the mechanism by which metformin may reduce OSCC cell proliferation is unknown.

Cyr61, commonly known as CCN 1, is a cysteine-rich angiogenic inducer found in the matrix. Cyr61/CTGF/Nov belongs to the CCN family of growth factors. Proliferation, differentiation, adhesion, migration, invasion, and angiogenesis are among the biological activities that Cry61 is involved in. Cyr61 is overexpressed in a variety of malignancies, including oral cancer. In addition, Cyr61 has been linked to poor clinical outcomes in a variety of cancer types. Metformin has been shown to suppress CCN1 signalling, which inhibits the invasive characteristics of pancreatic cancer cells16. In the instance of oral cancer, however, no such evidence has been found. The levels of pAKT and AKT expression in metformin-treated SCC25 cells were evaluated to investigate the influence of metformin on PI3K/AKT signalling.

The American Type Culture Collection (ATCC, USA) provided human oral squamous carcinoma cells (SCC25) and human embryonic kidney 293 (HEK293) cells. SCC25 and HEK293 cells were cultured in RPMI 1640 complete media supplemented at 37 °C in a humidified chamber. Santa Cruz Biotechnology provided Cyr61-specific siRNA and scrambled control siRNA. After ZA treatment, the SCC25 cell extract was collected using RIPA buffer. The expression of several proteins such as Cyr61, AKT, and pAKT was determined using Western blot analysis on both treated and untreated cells. Primary antibody dilutions were made according to the manufacturer's specifications.

In SCC25 cells, metformin therapy resulted in a significant reduction in pAKT levels. The overall level of AKT expression, however, did not change. Cyr61 expression was lowered significantly in cells treated with 10 mM metformin for 72 hours. Proliferation, adhesion, invasion, migration, and angiogenesis are all processes in that CCN1 is engaged in oral cancer cells.

Cyr61 has also been found to control the PI3K/AKT pathway in some cancer cells. Despite recent

technical advancements, oral cancer survival rates have only improved somewhat. Metformin treatment resulted in a significant reduction of cell viability in oral cancer cells SCC25 in both a dose and time-dependent way, according to new research. Metformin, on the other hand, had a rather minor inhibitory effect in the non-cancerous HEK-283 cell line. Metformin appears to have a specific inhibitory effect on OSCC cells, according to these findings. Metformin treatment reduced Cyr61 expression in OSCC cells in a dose- and time-dependent manner. The role of Cyr61 in the SCC25 cell line's viability was explored in this work. SCC25 cells lost their ability to survive after Cyr61 was knocked down using siRNA, according to this study.

Metformin can be used to treat both diabetes and cancer, as it is commonly recognized that diabetics have a very high risk of developing cancer. Despite the fact that this study only employed one cell model, further research using many more cell lines and in vivo evaluation of metformin could lead to the discovery of metformin as an anti-cancer medication for the treatment of oral cancer.

JOURNAL REFERENCE

Zhang, L., Q. Sun, Y. Ou, Q. Zhang and J. Hu, 2022. Metformin induces cytotoxicity in oral squamous cell carcinoma cells by targeting CCN1/Akt-axis. Int. J. Pharmacol., 18: 182-189.

KEYWORDS

Metformin, oral cancer, anticancer agent, oral squamous cell carcinoma, Cyr61, pAKT and AKT expression, PI3K/AKT pathway