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Therapeutic efficacy of short chain fatty acids against pancreatic cancer

Background: Pancreatic ductal adenocarcinoma (PDAC) is projected to become second leading case of cancer related deaths in the United States. Current treatments are less effective and resistance rates are high[1].

Short chain fatty acids (SCFA) are bioactive microbial metabolic products which are produced by the microbiota residing in the human digestive system. Among the SCFA produced by the intestinal microbiota, butyrate, propionate, and acetate are found in the highest concentrations[2]. SCFA have been found to function as histone deacetylase (HDAC) inhibitors which can have a wide range of effects on gene expression and show anti-cancer and anti-inflammatory properties. Butyrate in particular has been found to have anti-proliferative and pro-apoptotic effects on PDAC cell lines, but few studies have investigated the effects of other SCFA or a combination of them on PDAC cell lines in addition to chemotherapy.

Methods: Our study sought to investigate the effects of a combination of acetate, butyrate, and propionate on PDAC cell lines, and the combination of the SCFA treatment with chemotherapy in order to determine whether a synergistic effect occurred when used in combination. HS667T, MiaPaCa2, and PANC-01 PDAC cell lines were used in the experiments. The cells were seeded at a low density, treated with the SCFA combination only or the SCFA combination with FIRINOX chemotherapy, and the proliferation of the cells was monitored for 72 hours before conducting an MTS assay to assess cell viability.

Results: Preliminary results demonstrated a dose-dependent cytotoxic effect of the SCFA against the tumor cells. The dose-dependent antiproliferative effect was observed in the SCFA combination only treatment and in the SCFA with FIRINOX chemotherapy treatment groups. MTS assay results showed a dose-dependent decrease in cell viability when treated with SCFA combination alone and SCFA with chemotherapy in the HS766T cell line. MiaPaCa2 and PANC-01 preliminary results were inconclusive and further experiments should be conducted to optimize the protocol.

Conclusion: SCFA exerted a dose-dependent antiproliferative effect on tumor cells, and additional studies should be conducted to explore the mechanism responsible for the antiproliferative effects seen.

[1] Panebianco, C., Villani, A., Pisati, F., Orsenigo, F., Ulaszewska, M., Latiano, T. P., Potenza, A., Andolfo, A., Terracciano, F., Tripodo, C., Perri, F., & Pazienza, V. (2022b). Butyrate, a postbiotic of intestinal bacteria, affects pancreatic cancer and gemcitabine response in in vitro and in vivo models. Biomedicine & Pharmacotherapy, 151, 113163. https://doi.org/10.1016/j.biopha.2022.113163
[2] Mirzaei, R., Afaghi, A., Babakhani, S., Sohrabi, M. R., Hosseini-Fard, S. R., Babolhavaeji, K., Akbari, S. K. A., Yousefimashouf, R., & Karampoor, S. (2021). Role of microbiota-derived short-chain fatty acids in cancer development and prevention. Biomedicine & Pharmacotherapy, 139, 111619. https://doi.org/10.1016/j.biopha.2021.111619