Endocrine cancer treatment method using glycerate

Unmet Need

Endocrine cancers, those that affect organs that secrete hormones, are among the most common cancers in the U.S. Tumors that form in the organs of the endocrine system often secrete excess hormones or enzymes. This can cause severe discomfort including abdominal pain, anxiety, weight gain or loss, and lead to negative impacts on metabolism, growth, and can lead to death. In addition, many advance and late-stage adenocarcinoma manifest a loss of epithelial structure and show neuroendocrine differentiation that shares many characteristics with endocrine cancers. The main treatments for endocrine cancers are either severe and invasive such as surgery, chemotherapy, or radiation, or only modulate the disrupted hormone, such as with hormone therapy. Nonetheless, chemotherapy and hormonal therapy had limited success with treating these endocrine cancers. For example, current first-line treatment for insulinomas functions to alleviate symptoms of elevated circulating insulin, and prostate cancer with neuroendocrine phenotypes are castration-resistant. There is a need for a treatment method that directly inhibits the growth of endocrine cancers to target the disease in a less intrusive way and reduce the growth of tumors, not just inhibit the release of excess hormones.

Technology

Duke inventors have developed a treatment method to reduce tumor burden of endocrine cancers. This is intended for patients combating endocrine cancers, especially, insulinomas, small tumors formed from the beta cells of the pancreas, and adenocarcinomas with neuroendocrine phenotypes, such as small cell lung cancer and colorectal neuroendocrine cancer. Specifically, inventors propose using glycerate as a cell growth inhibitor for endocrine-lineage specific cell types, such as pancreatic beta cells. This has been demonstrated through *in vivo* experiments in which mice were injected daily with glycerate for 12 weeks and compared to those injected with fructose and saline control. The glycerate injected mice were found to have higher glucose intolerance by inhibiting insulin secretion. This result was due to reduced pancreatic beta cell content. Specifically, a reduction in islet diameter and an increase in apoptotic signaling were observed and localized to this region. These

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Links

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data suggest glycerate treatment affects pancreatic islets and reduces the number of beta cells. At the same time, the treatment has little to no cell death in other cells surrounding the pancreatic islets, making it an excellent therapy for targeting pancreatic tumors that overproduce beta cells. Additionally, *in vitro* and *in vivo* studies showed glycerate inhibits the growth of pituitary gland, lung, and colon cancer cells with neuroendocrine phenotypes.

Advantages

- Treatment method that targets cancerous endocrine cells to inhibit tumor growth (decreases cell proliferation and induce apoptosis) that does not require severe or invasive surgery
- *In vivo* and *in vitro* results show effectiveness of glycerate in decreasing the number and size of pancreatic beta cells and tumor burden of colorectal neuroendocrine cancer
- Inventors are developing a new glycerate-derivative compound to inhibit endocrine cancer tumor growth

Publications

- 713c Dietary Fat Increases Intestinal Fructose Conversion to Glycerate that Accumulates in Circulation, Driving Glucose Intolerance (Gastroenterology, 2021)