ICX-550 Induces Programmed Cell Death in Malignant Cells

Cancer treatment usually involves surgery in addition to radiation and chemotherapy. The chemotherapeutic agents that are being used are often not very effective and are toxic to both malignant and normal cells. Therefore, this study was conducted in order to find potential, chemotherapeutic agents that would be effective toward malignant cells but have minimal effects on normal cells. One of the candidates tested was a modified form of tryptamine, ICX-550. The rationale is that since tryptamine is a natural substance that is found in plants and animals and has, in the past, shown some anticancer activity, its use as a chemotherapeutic agent would yield minimal effects in humans. Therefore, the ability of ICX-550 to induce cell death was tested in normal (OK) and malignant (Daudi, SKMG) cells. Our results showed that acute treatment (1&10 mM; 24 hrs) of ICX-550 induced cell death in Daudi and SKMG cells, but not in OK cells. Chronic treatment with a lower dose of ICX-550 (100 nM; 7 day) induced apoptosis in Daudi and SKMG, but not in OK cells. Finally, chronic treatment with even lower doses of ICX-550 inhibits proliferation of malignant, but not normal cells. Therefore, ICX-550 is an excellent candidate as a chemotherapeutic agent that would be effective against malignant cells but has minimal effect on normal cells.

Student Researcher: Tyler Pearson, George Washington Carver High School; Birmingham, Alabama
Mentor: Tino Unlap, PhD, University of Alabama at Birmingham; Birmingham, Alabama

Introduction

Cancer is characterized by the abnormal proliferation of cells due to an induced defect in cell growth pathways. These cells eventually either proliferate into nearby tissues in a process of invasion or infect faraway sites in the body by way of metastasis, in which cells are carried through either blood vessels or the lymphatic system. These processes often result in degradation and death; cancer is one of the leading causes of death worldwide. Historically, cancer has been documented since the ancient Greek era, during which the disease was treated by a combination of various diets and bloodletting. These methods remained the main treatments until the 18th century, with the advent of surgery. Throughout the 18th and 19th centuries, surgery remained the main form of treatment for cancers of all types. Surgery continued to be the main form of treatment until modern times when radiation therapy and chemotherapy became treatment standards. Radiation therapy introduces the patient to high levels of radiation. While succeeding in killing cancer cells, this therapy has also been shown to damage healthy cells and is known to damage the immune system, placing patients at greater risk of infectious disease. Chemotherapy affects cells that grow quickly, leading to the common side effect of hair loss in patients. Cancer medications work through a variety of methods, including destruction of blood vessels which supply tumors, degradation of cellular DNA, inhibition of energy (ATP) and growth factor generation by cancerous cells, and induction of programmed cell death (apoptosis).

Methods

In order to conduct our experiment, cells were extracted from different areas of the body, which carried OK (kidney), Daudi (B-cell lymphoma) and SKMG (brain tumor) cells. These cells were incubated over a specific period of time. All cells were split and divided in six petri dishes and eight six-well plates. Cells were treated with ICX-550 and a diluted solution of the anticancer agent every other day.

Apoptosis in malignant cells was assessed by a process called FACS Analysis (fluorescent activity cell sorting) for acute and chronic treatments with confocal images. Acute treatments were treated at 1 and 10 mM for 24 hours. On days 1, 3, and 5 cells were treated and on day 7 apoptosis was assessed. Chronic treatments were treated at 1, 10 and 100 nM for 7 days. Confocal images were created to assess apoptosis among malignant cells with dyes Annexin-V FITC and propidium iodide. Cell proliferation was assessed using a hemacytometer. Cells were treated at concentrations of 1, 10, and 100 nM on days 1, 3, and 5. Cell proliferation was assessed on day 7.

Results

Our results showed that ICX-550 induced cell death in malignant, but not normal cells. In acute and chronic treatments, the effect of this drug had a significant percentage of apoptosis in both Daudi and SKMG cell lines. ICX-550 had a death-effect on both malignant (Daudi, SKMG) cells, but not on normal (OK) cells.

CONCLUSION

In conclusion, ICX-550 is a likely candidate as a chemotherapeutic agent that stimulates cell death in malignant cells, while not in normal cells. Also, ICX-550 can be used in other existing drugs by increasing their anticancer effects while also not having harmful side effects.

ACKNOWLEDGMENTS

The author thanks Dr. Tino R. Unlap for his time and assistance and the NIH Summer Research Program.

RESOURCES

Kobayashi Y, Itoh MT, Kondo H, et al. Melatonin binding sites in estrogen receptor-positive cells derived from human endomental cancer. *J Pineal Research*. 2003;35(2):71–74.

Paley EL. Tryptamine-mediated stabilization of tryptpphanyl-tRNA synthetase in human cervical carcinoma cell line. *Cancer Letters*. 1999;37(1): 1–7.