Association Between Breast Cancer and Diabetes

We evaluated the growth of estrogen receptor–positive breast cancer cells in media with different levels of glucose and cell response to tamoxifen treatment. Our results show that MCF7 breast cancer cells growing in higher levels of glucose do not have different responses to tamoxifen compared to breast cancer cells in normal growth conditions. However, we observed that MCF7 cells growing in higher levels of glucose medium tend to become estrogen independent and increase expression of cyclin D1 protein, which is a known cell cycle inducer.

Student Researcher: Erica Terrell;
Mentors: Jaydutt V. Vadgama, PhD; Yanyuan Wu, PhD;
Charles R. Drew University of Medicine and Science, Los Angeles, California

Introduction

Diabetes is a risk factor for several types of cancer, including endometrial cancer and pancreatic carcinoma.[1] Data suggest that type 2 diabetes might be associated with up to 10%–20% excess risk for breast cancer and that it could have detrimental effects on the natural history, diagnosis, and treatment of breast cancer.[2] Tamoxifen, a selective estrogen-receptor modulator, has been used to treat breast cancer. A significant number of patients with estrogen receptor–positive breast cancer eventually become resistant to tamoxifen treatment, but the reason for treatment resistance is unclear. This project uses MCF7 breast cancer cells that are maintained in a medium containing high glucose levels. These cells were used as a cell model to test if MCF7 breast cancer cells growing in higher levels of glucose have different responses to tamoxifen compared to breast cancer cells in normal growth conditions.

Methods

MCF7 breast cancer cells were grown in Dulbecco minimal essential medium F12 with 10% fetal bovine serum growth medium at 37°C and were infused with 2, 5, and 10 μmol/L tamoxifen for five days.

Cells were plated in 96-well plates containing Dulbecco minimal essential medium F12 and 10% fetal bovine serum. The number of treated cells at day 1 was considered 100%. The relative increase in cell number was determined after three, four, and five days of tamoxifen treatment. The levels of protein expression in cyclin D1 were measured by Western blotting. Beta-actin allowed us to determine if we were using equal loading controls.

Results

Tamoxifen inhibits MCF7 cell growth in 20 mmol/L glucose. Tamoxifen inhibits insulin-like growth factor 1 and insulin-induced cell growth in MCF7 cells. MCF7 cells grown in 20 mmol/L glucose are more likely to be estrogen independent. Cyclin D1 protein expression increased in MCF7 cells growing in 20 mmol/L glucose.

Discussion

When MCF7 cells were induced with insulin-like growth factor 1 and compared to the control MCF7 cells growing in 0% fetal bovine serum, we noted significant upregulation. However, when tamoxifen is included, MCF7 cell growth is inhibited. When insulin is induced in the MCF7 cells, it is also upregulated compared to the control MCF7 cells. However, when tamoxifen is supplemented, MCF7 cell growth is inhibited regardless of insulin. After comparing the effect of tamoxifen on cell growth, we conclude that it inhibits MCF7 cell growth in glucose. Moreover, MCF7 cells grown in glucose tend to be estrogen independent. Cyclin D1 protein expression increased in MCF7 cells grown in medium with 20 mmol/L glucose. Higher cyclin D1 leads to more cell proliferation. We conclude that MCF7 breast cancer cells grown in higher levels of glucose do not respond differently to tamoxifen compared to breast cancer cells

in normal growth conditions. However, they do become estrogen independent.

ACKNOWLEDGMENTS

The author thanks mentors Prof. Vadgama, Dr. Wu, Dr. Thant, and Dr. Chenfor for their help in this research project; the NIH/NIDDK program for this opportunity; the Division of Cancer Research and Training; and NIDDK students Ameachi Okafor, Carlos Guzman, Heather Garcia, and Juanita Soto.

REFERENCES

1. Czyzyk A, Szczepanik Z. Diabetes mellitus and cancer. *Eur J Intern Med.* 2000;11:245–252.
2. Wolf I, Sadetzki S, Catane R, Kaufman B. Diabetes mellitus and breast cancer. *Lancet.* 2005;6:103–111.