Cell Line Designation Change: Multidrug-Resistant Cell Line in the NCI Anticancer Screen

Since 1990, the Developmental Therapeutics Program (DTP) of the National Cancer Institute (NCI) has screened over 60,000 compounds and a larger number of natural product extracts for their capacity to inhibit the growth of 60 different human tumor cell lines. These cell lines have been maintained in cryopreservation and in culture, and they have been subjected to strict quality controls, including adventitious agent testing, human isoenzyme analysis, karyology, morphological and immunocytochemical characterization, and DNA fingerprinting. One of these cell lines, previously designated as MCF-7/ADR-RES, has been included in the in vitro cell line screening panel because of its stable multidrug-resistant (MDR) phenotype characterized by high levels of MDR-1 and P-glycoprotein expression. Recently, we submitted cell lines from the screening panel for DNA fingerprinting analysis by three different laboratories. Included in the tested cell lines were MCF-7 and MCF-7/ADR-RES. Utilizing restriction fragment length polymorphism (RFLP) testing, CellMark Diagnostics (Germantown, MD) concluded that their DNA fingerprinting data were consistent with each of the cell lines (MCF-7 and MCF-7/ADR-RES) having different donors. The other laboratories—American Type Culture Collection (Rockville, MD) used both RFLP and amplification fragment length polymorphism (AmpFLP) methods, and Children’s Hospital of Michigan Cell Culture Laboratory (Detroit, MI) used the AmpFLP method—reached the same conclusions. Based on the reports from these DNA fingerprinting analyses, we have concluded that the preponderance of the information available suggests that the MCF-7/ADR-RES multidrug-resistant cell line that is included in the DTP screening program is not related to the MCF-7 cell line that is a part of the screening panel. Thus, we have changed the nomenclature of the MCF-7/ADR-RES multidrug-resistant cell line. The new designation of this cell line is NCI/ADR-RES. This nomenclature change will soon appear in all DTP databases, including the worldwide web. The DTP website address is: http://epw1.ncifcrf.gov:2345/dis3d/dtp.html

Irrespective of its origin, this cell line has served as a valuable sentinel for compounds interacting with the multidrug-resistant mechanism.

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References


Notes

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Influence of Genistein and Daidzein on Brca1 Protein Levels in Human Breast Cell Lines

Phyto-estrogens potentially have anticarcinogenic biologic activities and could play a role in the dietary etiology of breast cancer. They have estrogenic as well as antianti-estrogenic properties and can also inhibit specific enzyme activities. In vitro and in vivo studies have shown that phyto-estrogens are tumor inhibitory. Moreover, Asian populations who consume large amounts of phyto-estrogens derived from a soy-rich diet have a lower frequency of breast tumors than western populations who consume much lower quantities of these compounds.

The BRCA1 gene is involved in breast cancer families with a pattern of autosomal-dominant inheritance of the disease. Comparison of BRCA1 messenger RNA levels in a series of normal breast tissues and sporadic breast cancer tissues demonstrated an apparent decrease in BRCA1 gene expression by tumor cells. Moreover, there is some evidence that BRCA1 gene transcription is directly and indirectly regulated by estrogen.

We investigated whether two selected phyto-estrogens—genistein and daidzein—modulate the expression of Brca1 protein in human breast cells. The effects of these phyto-estrogens were compared in three human mammary cell lines, MCF7 cells (estrogen receptor-positive cells), MDA-MB231 cells (estrogen receptor-negative adenocarcinoma-derived cells), and MCF10a cells (estrogen receptor-positive epithelial cells). Each cell line was treated for 96 hours at the IC50 of each phyto-estrogen—genistein (5 µg/mL) or daidzein (20 µg/mL).

For Brca1 protein determinations following either genistein or daidzein treatment, total cell extracts were prepared from cells metabolically labeled with [35S]methionine. Levels of Brca1 protein were determined by use of a magnetic protein purification protocol (Dynabeads M-450 coated with Brca1 antibodies D–20; Santa Cruz Biotechnologies, Santa Cruz, CA). The beads...