Distinct gene expression patterns in a tamoxifen-sensitive human mammary carcinoma xenograft and its tamoxifen-resistant subline MaCa 3366/TAM.

Max-Delbrueck-Center for Molecular Medicine, Experimental Pharmacology, Robert-Rössle-Strasse 10 D-13092 Berlin, Germany. mibecker@mdc-berlin.de

Abstract

The reasons why human mammary tumors become resistant to tamoxifen therapy are mainly unknown. Changes in gene expression may occur as cells acquire resistance to antiestrogens. We therefore undertook a comparative gene expression analysis of tamoxifen-sensitive and tamoxifen-resistant human breast cancer in vivo models using Affymetrix oligonucleotide arrays to analyze differential gene expression. Total RNAs from the tamoxifen-sensitive patient-derived mammary carcinoma xenograft MaCa 3366 and the tamoxifen-resistant model MaCa 3366/TAM were hybridized to Affymetrix HuGeneFL and to Hu95Av2 arrays. Pairwise comparisons and clustering algorithms were applied to identify differentially expressed genes and patterns of gene expression. As revealed by cluster analysis, the tamoxifen-sensitive and the tamoxifen-resistant breast carcinomas differed regarding their gene expression pattern. More than 100 transcripts are changed in abundance in MaCa 3366/TAM as compared with MaCa 3366. Among the genes that are differentially expressed in the tamoxifen-resistant tumors, there are several IFN-inducible and estrogen-responsive genes, and genes known to be involved in breast carcinogenesis. The genes neuronatin (NNAT) and bone marrow stem cell antigen 2 (BST2) were sharply up-regulated in MaCa 3366/TAM. The differential expression of four genes (NNAT, BST2, IGFBP5, and BCAS1) was confirmed by Taqman PCR. Our results provide the starting point for deriving markers for tamoxifen resistance by differential gene expression profiling in a human breast cancer model of acquired tamoxifen resistance. Finally, genes whose expression profiles are distinctly changed between the two xenograft lines will be further evaluated as potential targets for diagnostic or therapeutic approaches of tamoxifen-resistant breast cancer.

PMID: 15657362 [PubMed - indexed for MEDLINE]  Free full text