CHARACTERIZATION OF ANDROGEN RECEPTOR AND CO-FACTOR EXPRESSION IN HUMAN BREAST CANCER CELL LINES

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Accumulating evidence indicates that androgens and the androgen receptor (AR) play a significant role in the development and progression of breast adenocarcinoma; however, the precise role and actions remain ill-defined. We previously examined the steroid hormonal regulation of two known androgen-regulated genes, prostate specific antigen (KLK3 or PSA) and human glandular kalikrein 2 (KLK2) in several breast cancer cell lines (BT-474, T-47D, ZR-75-1, MCF-7, MFM-223, BT-20) and found that they were differentially regulated with the cells showing variable responses to androgens. To determine if this variable response was reflected by differences in AR, we characterized the expression of AR by RT-PCR, Western blot analysis, and saturation binding analysis.

In addition, we sequenced AR cDNA from each of these cell lines to determine if AR mutations were present.

AR expression was detected in all cells lines by RT-PCR with the exception of BT-20 cells. Western blot analysis revealed a 110 kDa immunoreactive band for the same cell lines. Saturation binding analysis indicated the presence of a single high affinity binding site (Kd = 0.1-0.2 nM), with concentrations ranging from 20 fmol/mg cytosol protein in MCF-7 cells to 145 fmol/mg in MFM-223 cells. No binding was detected in BT-20 cells. No mutations within the AR coding sequence were detected; however, variations in the number of CAG repeats in the polymorphic region of exon 1 were observed. RT-PCR was used to screen the cell lines for the expression of a number of AR co-factors (Src-1, AIB1, ARA24, ARA160, ARA 70, ARA54, ARA55, PHL2, SMRT and NCoR1). These were found to be present in variable amounts between the cell lines. In conclusion, non-mutated AR are expressed in the human breast cancer cell lines tested. Differences in the levels of the receptor as well as of many AR co-factors may be responsible for the differential regulation of PSA and KLK2 by androgens in these cells.