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ESTROGEN RECEPTOR β AND AS A POSSIBLE BIOMARKER OF TAMOXIFEN RESISTANCE

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Introduction: Approximately two-thirds of all breast cancer patients overexpress hormonal receptors and are treated with endocrine therapy, being tamoxifen (TAM) the standard treatment. However, many of the initial responders to TAM as first-line experience relapse. Several mechanisms have been proposed to explain the occurrence of acquired TAM resistance. Previous studies showed that estrogen receptor β (ERβ) expression is associated with better response to tamoxifen treatment, as the co-expression of ERα and ERβ is associated with TAM antiproliferative effects. Moreover, there is a growing interest about the cross talk between ERs and ErbB family in response to endocrine therapy. **Objectives:** The aim of the present study was to evaluate the expression of ERβ and the relation of ERβ with ERα and ErbB family in response to TAM treatment and in TAM resistant cells. **Methods:** ERβ expression was analyzed in two different databases of breast cancer patients. The mRNA levels of ER, HER receptors and PTEN and MAPK signal pathways were measured after TAM treatment, in TAM resistance cells and in cells silenced for ER genes. The cellular viability was also measured after TAM treatment, in TAM resistance cells and in cells silenced for ER genes. **Results:** Breast cancer patients presented reduced ERβ expression, and the ERα-positive breast cancer subtypes presented lower ERβ levels when compared to ERα-negative breast cancer subtypes. Cells expressing moderate levels of ERβ presented a better response to TAM treatment. Downregulation of ERs induced by TAM treatment was accompanied by an increase in ErbB2 and ErbB3, MAPK3 mRNA levels and increased PTEN levels. TAM–resistant cells expressed decreased ERs, PTEN and MAPK3 mRNA levels and increased EGFR, ErbB3 and ErbB4 levels. In accordance to the resistance finding, cells silenced for ERβ presented decreased MAPK3 and cells silenced for ERα showed an increased EGFR. **Conclusions:** These results provide additional data indicating the importance of ERβ as a possible biomarker of endocrine resistance and highlighted the interaction between ERα and EGFR as a mechanism of TAM resistance.