題名:Increased expression of enolase in human breast cancer confers tamoxifen resistance in human breast cancer cells

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摘要:Enolase-alpha (ENO-1) is a key glycolytic enzyme that has been used as a diagnostic marker to identify human lung cancers. To investigate the role of ENO-1 in breast cancer diagnosis and therapy, the mRNA levels of ENO-1 in 244 tumor and normal paired tissue samples and 20 laser capture-microdissected cell clusters were examined by quantitative real-time PCR analysis. Increased ENO-1 mRNA expression was preferentially detected in estrogen receptor-positive (ER+) tumors (tumor/normal ratio >90-fold) when compared to ER-negative (tumor/normal ratio >20-fold) tumor tissues. The data presented here demonstrate that those patients whose tumors highly expressed ENO-1 had a poor prognosis with greater tumor size (>2 cm, *P = .017), poor nodal status (N > 3, *P = .018), and a shorter disease-free interval (<==1 year, *P < .009). We also found that higher-expressing ENO-1 tumors confer longer distance relapse (tumor/normal ratio = 82.8-92.4-fold) when compared to locoregional relapse (tumor/normal ratio = 43.4-fold) in postsurgical 4-hydroxy-tamoxifen (4-OHT)-treated ER+ patients (*P = .014). These data imply that changes in tumor ENO-1 levels are related to clinical 4-OHT therapeutic outcome. In vitro studies demonstrated that decreasing ENO-1 expression using small interfering RNA (siRNA) significantly augmented 4-OHT (100 nM)-induced cytotoxicity in tamoxifen-resistant (Tam-R) breast cancer cells. These results suggest that downregulation

of ENO-1 could be utilized as a novel pharmacological approach for overcoming 4-OHT resistance in breast cancer therapy.