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Epidermal growth factor receptor pathway gene expressions and biological response of glioblastoma multiforme cell lines to erlotinib.

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BACKGROUND: Erlotinib, an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, exerts highly variable antiproliferative effects on human glioblastoma multiforme (GBM) cells in vitro and in vivo. As these effects are independent of EGFR baseline expression levels, more complex genetic signatures may form the molecular basis of the erlotinib-sensitive and erlotinib-resistant GBM phenotypes. The aim of the current study was to determine which genes within the EGFR signaling pathway are candidates for mediating the cellular response of human GBM towards erlotinib. **MATERIALS AND METHODS:** Complementary (c)RNAs from cell lines selected to represent the sensitive, intermediately responsive and resistant phenotypes, respectively, were hybridized to CodeLink Human Whole Genome Bioarrays. **RESULTS:** Expression analysis of the prospectively selected 244 genes whose products constitute the EGFR signaling pathway identified five genes the expression of which significantly correlated with phenotype. Functional annotation analysis revealed one (STAT1) and two (FKBP14, RAC1) genes conclusively associated with sensitivity and resistance to erlotinib, respectively. Moreover, two additional genes (PTGER4, MYC) were unexpectedly found to be associated with sensitivity. The gene expressions were confirmed by quantitative polymerase chain reaction. **CONCLUSION:** Five genes within the EGFR signaling pathway may modulate GBM response to erlotinib, which further emphasizes the importance of this pathway for the biology of GBM.

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