Determinants of erlotinib and pemetrexed synergism in non-small cell lung cancer (NSCLC) cell lines

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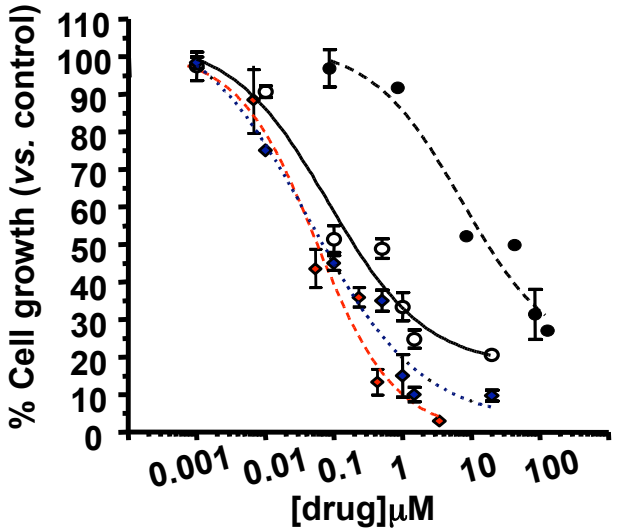
Rationale and aim of the study

1) Erlotinib shows clinical activity in NSCLC

2) Pemetrexed is a standard treatment for second line NSCLC, which
- may induce EGFR expression
- may modulate Akt or MAPK activity
- affects TS, whose activity may be influenced by EGFR-TKIs

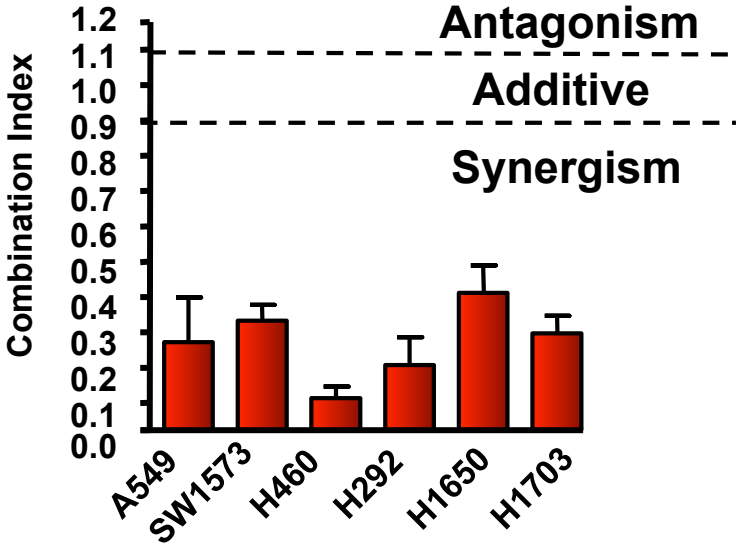
the aim of this study was to evaluate the molecular mechanisms underlying the pharmacologic interaction between erlotinib and pemetrexed in NSCLC cells

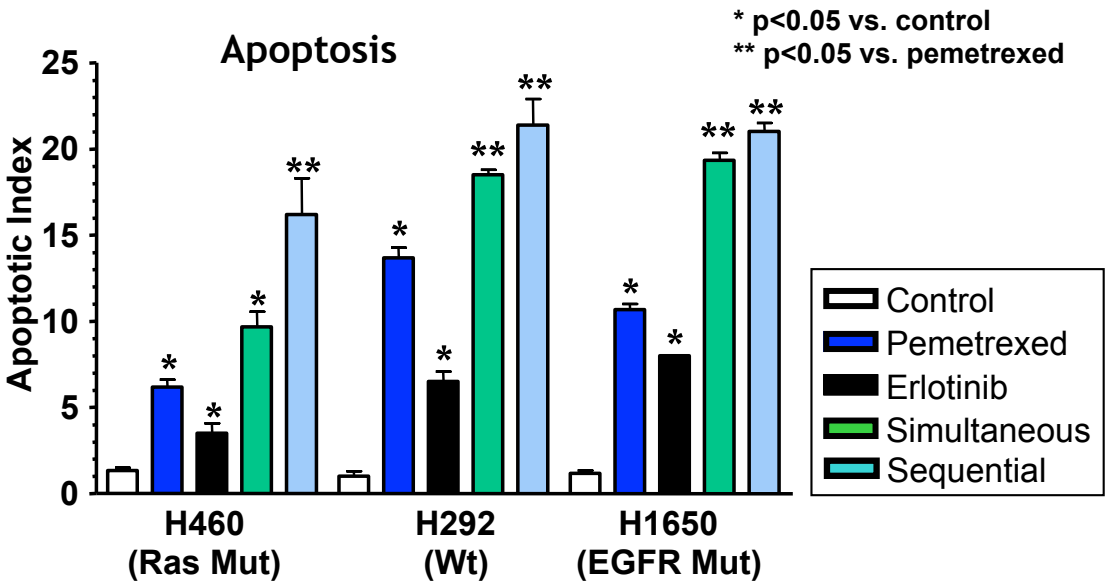
Results (1)

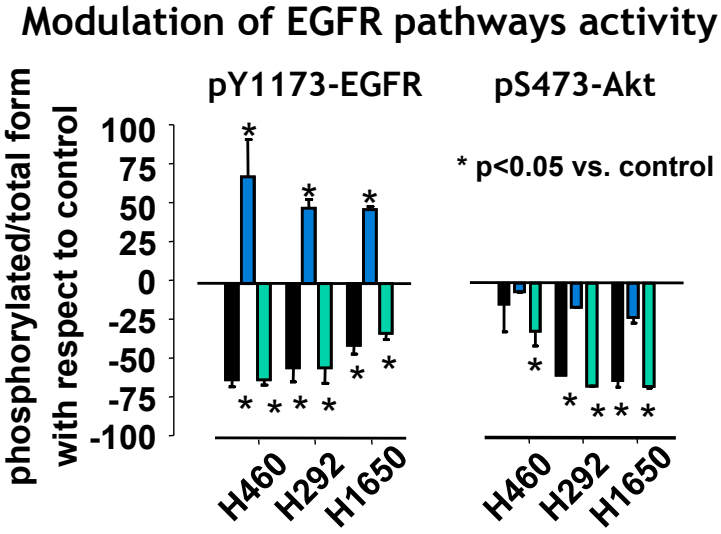


Pharmacological Interaction

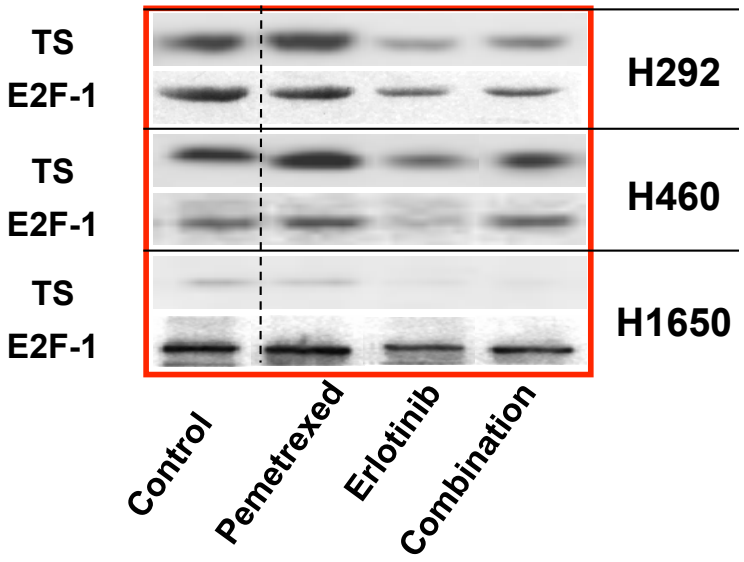
- Erlotinib
- Pemetrexed
- Simultaneous combination
- Sequential combination

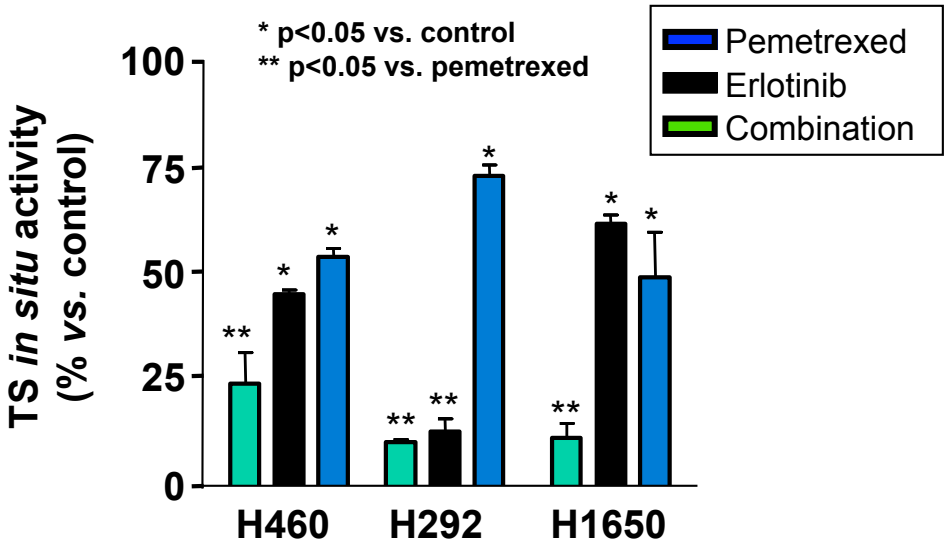






Results (2) and Conclusions





- Synergism was most pronounced with pemetrexed (PMX) pretreatment
- Synergism was associated with significant induction of apoptosis
- PMX increased EGFR and reduced Akt phosphorylation
- Erlotinib reduced E2F-1 and TS expression, enhancing PMX-mediated TS inhibition

PMX-erlotinib combination should be further developed for treatment of NSCLC