Ursolic Acid Effectively Synergizes with Erlotinib to Suppress Non-small Cell Lung Cancer Cell Proliferation, Invasion and Migration by Inhibiting EGFR Expression

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Purpose
Molecular therapies targeting epidermal growth factor receptor (EGFR) have had a profound impact on the management of advanced non-small cell lung cancer (NSCLC). However, the emergence of resistance to EGFR inhibitor therapy is a major clinical problem for patients. There is a need for additional therapeutic approaches for NSCLC. The present study aimed at elucidating the combination effect of ursolic acid (UA) and erlotinib, a tyrosine kinase inhibitor on the cell proliferation, invasion and migration in NSCLC cells.

Methods
MTT assay was used to evaluate the cytostatic effects of UA, Erlotinib, and two-drug combinations (UA+El) in A549 (wild-type EGFR) and H1975 (mutated-type EGFR) two NSCLC cell lines. Transwell chamber assay was used to measure the ability of NSCLC cells motility. Expression of metastasis-related proteins was determined by western blot assay.

Results
UA+El had lower toxicity effect in both A549 and H1975 cells (Fig. 1, 2). UA+El effectively inhibited the invasion of A549 cells at non-cytotoxic concentrations (Fig. 3, 4). UA+El significantly down-regulated the expression of EGFR proteins (Fig. 5, 6).

Conclusion
Overall, the results demonstrated that two-drug combinations UA+El had a synergistic inhibition effect on the invasion and migration in both NSCLC cell lines with either wild (A549) or mutated EGFR (H1975). It provides a novel approach to overcome erlotinib resistance by suppressing the EGFR protein expression in human NSCLC. [This project was supported by the Natural Science Foundation of Fujian Province of China (2014J01364)].