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### Enhancement of gefitinib-induced growth inhibition by *Marsdeniastenacissima* extract in non-small cell lung cancer cells expressing wild or mutant EGFR

Shuyan Han

Peking University Cancer Hospital & Institute, PR China

Gefitinib has demonstrated clinical efficacy in NSCLC patients harboring EGFR mutations or refractory to chemotherapy. However, most of NSCLC patients are with wild type EGFR, and had limited response to gefitinib. The previous study showed *Marsdeniastenacissima* extract (MTE) restored gefitinib efficacy in the resistant NSCLC cells, but whether MTE acts in the sensitive NSCLC cells is the same as it in the resistant one is unknown. Three different sequential combinations of MTE and gefitinib on cell growth were evaluated using IC<sub>50</sub> and Combination Index approaches. The flow cytometric method was used to detect cell apoptosis and cell cycle profile. The impact of MTE combined with gefitinib on cell molecular network response was studied by Western blotting. Unlike in the resistant NSCLC cells, results revealed that three different schedules of MTE combined with gefitinib synergistically or additively enhanced the growth inhibition of gefitinib. Among which, MTE → MTE + gefitinib treatment was the most effective one. The Western blotting results showed that MTE → MTE + gefitinib treatment further enhanced suppression of ERK1/2 and PI3K/Akt/mTOR pathway. This combination also blocked the activation of EGFR and c-Met which have cross-talk with each other. Unlike in gefitinib-resistant NSCLC cells, MTE alone also demonstrated certain unexpected modulation on EGFR related cell signal pathways in the sensitive cells. Obtained results suggest that MTE is a promising herbal medicine to improve gefitinib efficacy in NSCLC regardless of EGFR status.

#### Biography

Shuyan Han has completed her PhD from Peking University in 2008, and did postdoctoral studies from Peking University Cancer Hospital & Institute. Now she is an Associate Professor and Master supervisor in Peking University Cancer Hospital & Institute. Her area of research interests are efficacy evaluation and mechanisms elucidation of anti-cancer herbal medicine, overcoming drug resistance by integrative medicine. She has published more than 25 papers in reputed journals.

shuyanhan@126.com