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# EGF induces paradoxical growth arresting via the up-regulation of PTEN by activating Ref-1/Egr-1 in human NSCLC cells

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Epidermal growth factor receptor (EGFR) signaling promotes cell proliferation and survival in several types of cancer. Here, however, we showed that EGF inhibits proliferation and promotes apoptosis in non-small cell lung cancer (NSCLC) cells. In A549 cells, EGF increased redox factor-1 (Ref-1) expression and the association of Ref-1 with zinc finger-containing transcriptional regulator (EGR1) via activation of $p22^{phox}$, RAC1 and an NOX subunit. EGF increased $p22^{phox}$ and RAC1 expression through activation of purinergic receptors (P2Y). Elevated Ref-1/EGR1 levels increased phosphatase and PTEN levels, leading to inhibition of the Akt pathway. EGF-induced PTEN up-regulation increased apoptosis and autophagy-induced damage in A549 cells, whereas Ref-1 knockdown blocked EGF-induced PTEN up-regulation in an NOX -$p22^{phox}$ subunit-independent manner. In addition, $p22^{phox}$ knockdown restored EGF-induced effects, implying that changes in P2Y activity caused by EGF, which activates NOX via RAC1, influenced Ref-1-mediated redox regulation. Finally, EGF similarly attenuated cell proliferation and promoted autophagy and apoptosis in vivo in a xenograft model using A549 cells. These findings reveal that EGF-induced redox signaling is linked to Ref-1-induced death in NSCLC cells.

## Biography

In-Hye Jung has completed her MSc from University of Ulsan College of Medicine. She is the Fellow in Department of Radiation Oncology of Asan Medical Center.

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