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Conference Abstract

Synthetic epidermal growth factor receptor (EGFR)-mitochondria desired axles-based split green-fluorescent-protein (GFP) could screen for the signaling molecules that overcome the drug resistance to tyrosine kinase inhibitor (TKI)

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Abstract

Background

The epidermal growth factor receptor (EGFR) pathway, involving in cancer cell migration, proliferation, and survival, attracts lots of attention of cancer biologists for seeking therapeutic targets. Tyrosine kinase inhibitor (TKI)-resistance of small cell lung cancer and cancer stem cells, the sub-population with EGFR mutations, has been associated with frustrating outcomes for anti-EGFR-based therapy.

New information

Methods & Results

With our synthetic EGFR-mutant axles that enlightened mitochondria, the small-cell lung cancer CL1-0 cell line interestingly revealed good correlation of the activated EGFR or spontaneously activated EGFR mutant T790M/L858R with high energy-demanding status. The facts implied that EGFR signaling might induce mitochondria proliferation to meet cellular energy demand by an unknown mechanism. The activated EGFR resulted in elevated MMP7 expression and further induced mitochondria proliferation in multiple cell lines. Therefore, enzymatically dead mutant MMP7 N-GFP fusion protein could be used as baits to screen for the putative substrates that modulate signals transduction from EGFR to mitochondria proliferation.

Conclusion

This synthetic cellular model platform could screen for a variety of mitochondria-targeting molecules, such as mitochondria ATP synthetase inhibitor, namely compound X, in lung cancer cells in cooperation with Gefitinib, a widely used TKI, to see whether it may increase the efficacy of Gefitinib on the resistant cells by cutting off energy supply in mitochondria.

Keywords

mitochondria, epidermal growth factor receptor, tyrosine kinase inhibitor, matrix metalloproteinase-7

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