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High intracellular cholesterol level reduces the sensitivity to EGFR-TKI therapy may via ABCA1 in NSCLC harboring EGFR mutations

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Cancer cells need excess cholesterol to maintain a high level of proliferation is well accepted, however why intracellular cholesterol level is high in epidermal growth factor receptor-tyrosine kinase inhibitors resistance in non-small cell lung cancer harboring EGFR mutations has not been elucidated. To explore this relationship, we utilized an EGFR-TKIs sensitizing EGFR exon 19 deletion (ΔE746-A750) PC-9 cells and gefitinib-resistant PC-9/GR and H1975 cells by cholesterol assay kit to compare the cholesterol level between gefitinib-sensitizing and gefitinib-resistant cells. By means of polymerase chain reaction (PCR) and western bolt detected the ATP-binding cassette transporters level. ABCA1 knockdown by siRNA in gefitinib resistant cell lines PC-9/GR and H1975, MTT was determined the growth rate. We found that in gefitinib-resistant cells, the cholesterol level and ABCA1 expression were remarkably higher than gefitinib-sensitizing cells. Furthermore, ABCA1 knockdown by siRNA in gefitinib resistant cell lines restored the sensitivity of gefitinib, reduced the intracellular cholesterol level and significantly inhibited the downstream signal pathways. Our results demonstrate that higher cholesterol level contributes to Gefitinib resistance which may due to ATP-binding cassette transporters A1 expression change in NSCLC cells.

Biography

Pan Zhenzhen is a graduate of Clinical Pharmacy at China Pharmaceutical University and has completed his undergraduate studies at Chongqing Medical University. She has published a paper in SCI as a second author.

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