Results: The resistance indexes of A549/Gem and H460/Gem are stably about 120 respectively which had exceeded 160 before had acquired steady gemcitabine resistance in the process of inducement. Expression of CDA, RRMI, PTEN and ERCC1 varies according to the changing trend of resistance indexes of gemcitabine, but expression of dCK does not change apparently. Since wild type promotor can amplify the frequency of genome in different devirational stages of A549/Gem and H460/Gem, but allelotype not, the gene type of A549/Gem, H460/Gem and their parental cells are still wild type.

Conclusion: Compared with their parental cells, expression of CDA, RRMI, PTEN and ERCC1 in human gemcitabine-resistant non-small cell lung cancer cell lines A549/Gem and H460/Gem rise, and dCK change is not obvious; the gene type of them are all wild type.

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Establishments of gemcitabine-resistant cell lines A549/Gem and NCI-H460 and studies about their biological characters

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Background: To establish human gemcitabine-resistant non-small cell lung cancer cell lines and discuss their biological characters so as to elaborate the possible mechanisms of gemcitabine resistance.

Methods: Two human Gemcitabine-Resistant non-small cell lung cancer cell lines A549/Gem and H460/Gem were established by repeated clinical serious peak concentration then low but gradually increasing concentration of gemcitabine and 2/3 clinical serious peak concentration gemcitabine intermittent selection from their parental cells human lung adenocarcinoma cell line A549 and human large cell lung canceroma cell line NCI-H460 who are sensitive to gemcitabine respectively. During the course of inducement, we had monitored their morphol-ogy, checked their resistance indexes and resistant pedigree by MTT method, gathered their growth curves and calculated their doubling time, examined their DNA contents and cell cycles by FCM; at the same time, we had measured their expression of P53, EGFR, c-erb-B-2, PTEN, PCNA, c-myc, VEGF, MDR-1, Bcl-2, nm23, MMP-9, TIMP-1 and CD44v6 Proteins.

Results: The resistance indexes of A549/Gem and H460/Gem to gemcitabine are 1.644 and 129.783, respectively, and the cell lines also exhibits respectively cross-resistance to vinorelbine, docetaxel, etoposide, cisplatin and taxol, etoposide, cisplatin. Compared with their parental cells, A549/Gem and H460/Gem are mixed with giant cells of different sizes that are larger and more irregular. The doubling time of A549/Gem is shorter and figures in G0-G1 phase are increased. Meanwhile, H460/Gem have developed contrary changes. Furthermore, they produced different results in different checkpoints. The farther studies indicated that compared with A549, PTEN expression of A549/Gem had been (-) and then rises, MMP-9 expression rises, EGFR TIMP-1 and c-myc (+), P53 c-erb-B-2 and bcl-2 drops, nm23 rises and then (-), and PCNA, MDR-1 (-). Compared with NCI-H460, H460/Gem had exhibited TIMP-9 (+) and P53 CD44v6 (+), then c-erb-B-2 (+), increased expression of nm23 bcl-2 MDR-1 and decreased expression of MMP-9 VEGF P53.

Conclusion: The human gemcitabine-resistant non-small cell lung cancer cell lines A549/Gem and H464/Gem have achieved multi-drug resistance and great changes of biological characters compared with their parental cells. And these changes possibly participate in the formation of multidrug resistance.