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Establishment and biological characteristics of a multi-drug resistant cell line A549/Gem

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摘要

Background and objective Multi-drug resistance is one of the most important reason why the survival time of non-small cell lung cancer patients is so short. The aim of this study is to establish multi-drug resistant cell line A549/Gem and discuss its biological characters so as to elaborate the possible mechanisms of gemcitabine resistance. Methods Human gemcitabine-resistant non-small cell lung cancer cell line A549/Gem was established by repeated clinical serous peak concentration then low but gradually increasing concentration of gemcitabine from its parental cell human lung adenocarcinoma cell line A549 which is sensitive to gemcitabine. During the course of inducement, monitored its morphology, checked its resistance index and resistant pedigree by MTT method, gathered its growth curve and calculated its doubling time, examined its DNA contents and cell cycles by flow cytometry; at the same time, measured its expression of P53, EGFR, c-erb-B-2, PTEN, PCNA, c-myc, VEGF, MDR-1, Bcl-2, nm23, MMP-9, TIMP-1, CD44v6 Proteins, and RRM1 mRNA. Results The resistance index of A549/Gem?to gemcitabine was 163.228, and the cell line also exhibited cross-resistance to vinorelbine, taxotere, fluorouraci, etoposide and cisplatin, but kept sensitivity to paclitaxol and oxaliplatin. The doubling time of it was shorter and figures in G0-G1 phase were increased than A549. Compared with A549, A549/Gem?achieved EGFR and c-myc protein expression, nm23 protein expression enhanced, p53, Cerb-B-2 and bcl-2 protein expression reduced, PTEN, PCNA and MDR-1 protein expression vanished, but that of MMP-9, VEGF, CD44v6 and TIMP-1 protein changed trivially. Meanwhile, the expression of RRM1 mRNA was augmented markedly. The resistance index
of A549/Gem to gemcitabine was 129.783, and the cell line also held cross-resistance to vinorelbine, taxotere, etoposide, cisplatin and sensitivity to paclitaxol. But the resistance to fluorouracil and sensitivity to oxaliplatin vanished. And the expression of RRM1 mRNA decreased visibly. The doubling time of A549/Gem was longer and figures in G0-G1 phase were decreased than A549/Gem'. It's expressions of P53, EGFR, PCNA and MDR-1 protein was same to that of A549/Gem?. A549/Gem achieved TIMP-1 and PTEN protein expression, Cerb-B-2, MMP-9, cmyc
and bcl-2 protein expression enhanced, nm23 protein expression vanished, but the expression of VEGF and CD44v6 protein changed trivially. Furthermore, Compared with its parental cell, A549/Gem was mixed with giant cells of different sizes that were larger and more irregular. Conclusion The multi-drug resistant non-small cell
lung cancer cell line A549/Gem has multi-drug resistance and great change of biological character compared with its parental cell. And the change can participate in the formation of multidrug resistance.

关键词

Gemcitabine;Drug resistance;Non-small cell lung cancer;Gene

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