P.21 ERCC1 expression and platinum-based chemotherapy efficacy in ovarian cancer patients
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INTRODUCTION

Platinum drugs are effective and most often used in ovarian cancer treatment. Their mechanism of action is associated with DNA damage through mono-adducts formation and, as a result, intra- and inter-DNA crosslinks. ERCC1 is a key protein of nucleotide excision repair system and a potential predictor of response to the platinum-based chemotherapy. The study goal was to quantify ERCC1 expression in ovarian cancer and estimate a correlation of this molecular marker to the platinum-based therapy efficacy.

RESULTS AND DISCUSSION

Immunofluorescent analysis of ERCC1 expression using flow cytometry

Immunofluorescent estimation of ERCC1 expression was quantified by flow cytometry in 37 surgical serous ovarian adenocarcinoma samples. Antibodies to ERCC1 (ab2356), isotypic (ab18415) and FITC-labeled secondary antibodies (Sigma F2772) were used. Mean cell fluorescence (expression intensity) and number of stained cells (expression level) were analyzed with WinMDI software and Kolmogorov-Smirnov approach. Integral index of ERCC1 expression calculated by multiplying the level and intensity of ERCC1 expression was used for correlation to the platinum-based therapy efficacy.

![Expression level](image1)

**Expression level**

![Expression intensity](image2)

**Expression intensity**

![Integral index of expression](image3)

**Integral index of expression**

Fig.1 Characteristics of ERCC1 expression in ovarian cancer tissue.

Different levels of ERCC1 expression (48–72%) with widely variation in expression intensity and integral index (3-30) were revealed in the patients investigated. Based on the clinical data about platinum-based chemotherapy efficacy nearly 40% of ovarian cancer, the investigated patients were divided into potentially sensitive and resistant (40 and 60% respectively) with integral index of ERCC1 expression less or more 15 respectively. Clinical efficacy of carboplatin-paclitaxel therapy (disease recurrence in 6 months or after 12 months after finish of the last chemotherapy course) was evaluated in real time in 8 patients. Three primary tumors sensitive to the chemotherapy had integral index of ERCC1 expression 9, 11 and 14, but resistant ones – 16 and 30. In recurrent tumors integral index of ERCC1 expression was 25 and 30. In one case only the ERCC1 resistant phenotype did not predict chemotherapy resistance of primary tumor.

![Resistant phenotype](image4)

**Resistant phenotype**

![Sensitive phenotype](image5)

**Sensitive phenotype**

Fig.2 Examples of histograms demonstrating the resistant and (a, b) and sensitive (c, d) tumor phenotype in accordance with ERCC1 expression index.

The fluorescence intensity (arbitrary units) is plotted along the abscissa; the number of cells, along the ordinate. Shaded histograms represent the distribution of cells after incubation with isotypic antibodies; unfilled histograms, after incubation with specific antibodies to ERCC1. Arrows on the figure indicate ERCC1 expression index (multiplication of expression level and expression intensity): resistant phenotype – 22.9 and 25.2; sensitive phenotype – 8.6 and 12.4.

CONCLUSION

Quantitative estimation of ERCC1 expression in ovarian cancer tissue revealed significant molecular heterogeneity of histological similar malignancies – serous ovarian adenocarcinoma and inverse correlation integral index of ERCC1 expression and carboplatin-paclitaxel chemotherapy efficacy.

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LITERATURE