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Genomic markers for ovarian cancer at chromosomes 1, 8 and 17 revealed by array CGH analysis

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ABSTRACT

Aims and background. The literature data show that the most frequently affected chromosomes in ovarian carcinogenesis are 1, 8 and 17. In the present study we aimed to define more precisely at a high resolution the genomic imbalances of these chromosomes in ovarian cancer and to determine genomic markers separating tumors of different histological types and stages.

Methods. Array comparative genomic hybridization (CGH) with a resolution of ≈0.8 Mb was applied in 28 primary ovarian tumors. We identified regions of highly frequent gains or losses (affecting more than 40% of ovarian cancers) and determined sites showing alterations of elevated amplitude (amplifications or homozygous deletions). Doing this we also identified at least two adjacent changed clones.

Results. We determined anomalies strongly associated with the disease such as deletions at 8p21-23, 17p12-13, 1p35-36 or amplifications at 1q23, 17q12, 17q23.2, 8q13.2, 8q24. We defined more precisely the gains in 17q12-q24, finding as strong candidates for ovarian tumorigenesis the genes LASP1 (17q12), TGF11 (17q21.32), MUL (17q23.2), TBX2 (17q23.2), AXIN2 (17q24.3) and GRB2 (17q25.1). Of particular note was gain of 8q13.2, which occurred at a high frequency in ovarian cancer, especially in serous and late-stage tumors. We found that gains of 1q32-1q43, 8p11-p12, 8q11.23, 8q13.2, and 8q24.21-8q24.22 and losses of 1p36.21, 8p23.1-8p21.1 and 8q21.2 were associated with serous histology, whereas losses of 1q23 and 1q32-43 and gains of 17q11.2-12 and 17q25 were associated with mucinous histology. Gains of 1q23, 8q24, 17q23.2, 17q24.2 and losses of 1p35-36, 8p, 17p, and 17q were specific for late-stage ovarian cancers.

Conclusions. Our study has identified potential genomic markers of interest on chromosomes 1, 8 and 17 in ovarian cancer. Tumors showed a wide variety in the patterns of alteration, suggesting that alternative mechanisms of genomic instability may play a role in this tumor type.

Key words: ovarian cancer, array CGH, genomic instability, oncogenes.

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