—Photogravure—

Comparative Genomic Hybridization Analysis of Cisplatin-Resistant Ovarian Carcinoma Cells

Ritsuko Arai, Mohammad Ghazizadeh and Oichi Kawanami

Department of Molecular Pathology, Institute of Gerontology,
Postgraduate School of Nippon Medical School

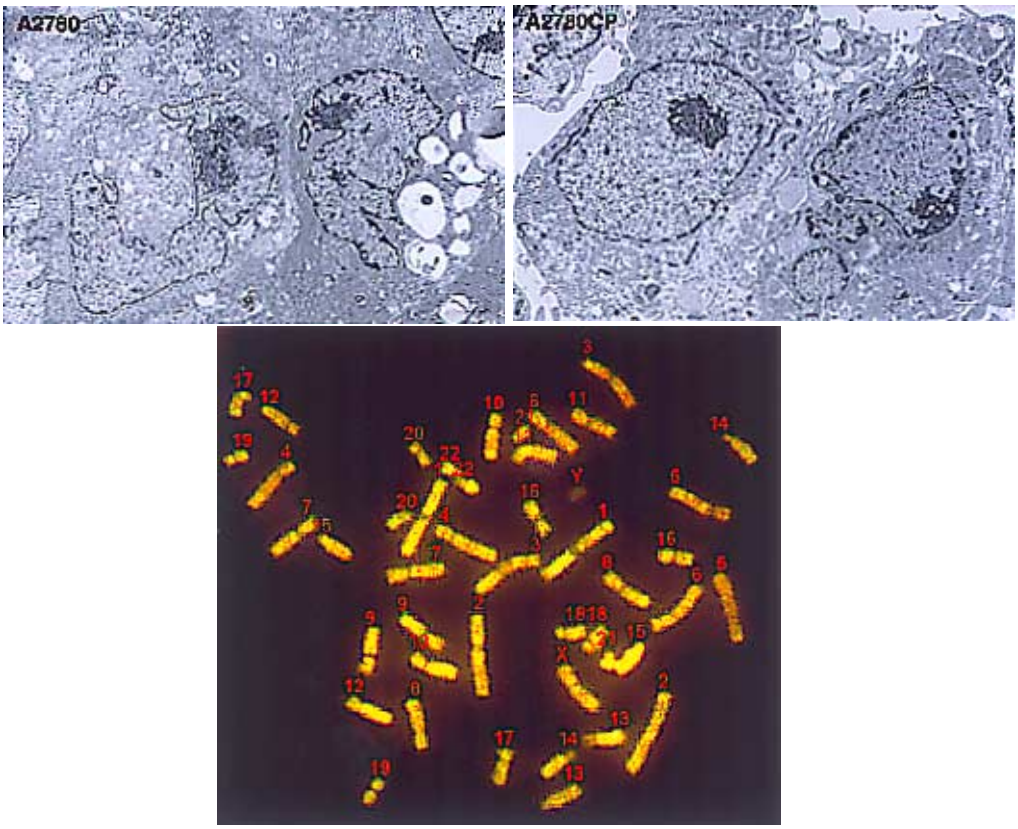

Fig. 1

Chromosomal gains and losses of DNA materials were examined in a cisplatin-resistant ovarian carcinoma cell line (A2780CP) compared to its parental cell line (A2780) by comparative genomic hybridization (CGH). DNA from each cell line was labeled with spectrum-green fluorescence, while normal reference DNA was labeled with spectrum-red fluorescence. A mixture of paired normal reference and tumor cell DNA probes at 1:1 proportion was hybridized to normal metaphase chromosome spreads. Using Leica Q-FISH and Q-CGH image analysis system (Leica, Wetzlar, Germany), the fluorescence images of each chromosome pair with intensity ranges between red and green were acquired and quantified. Accordingly, an increased green to red ratio indicated gains of DNA material, while a decreased ratio represented losses of DNA material in the tumor cells at the specific chromosome regions.

Fig. 1 (*Upper*) Electron micrographs of cisplatin-resistant ovarian carcinoma cell line (A2780CP) and its parental cell line (A2780). No significant morphologic change between the two cell variants is observed. (*Lower*) Fluorescence image of a metaphase chromosome spread after hybridization with a probe mixture of equal normal reference DNA and DNA from A2780CP cells.
Note that green fluorescence indicates gains, and red fluorescence losses of DNA materials in A2780CP cells.

e-mail: rarai@nms.ac.jp
Journal Website (http://www.nms.ac.jp/jnms/)

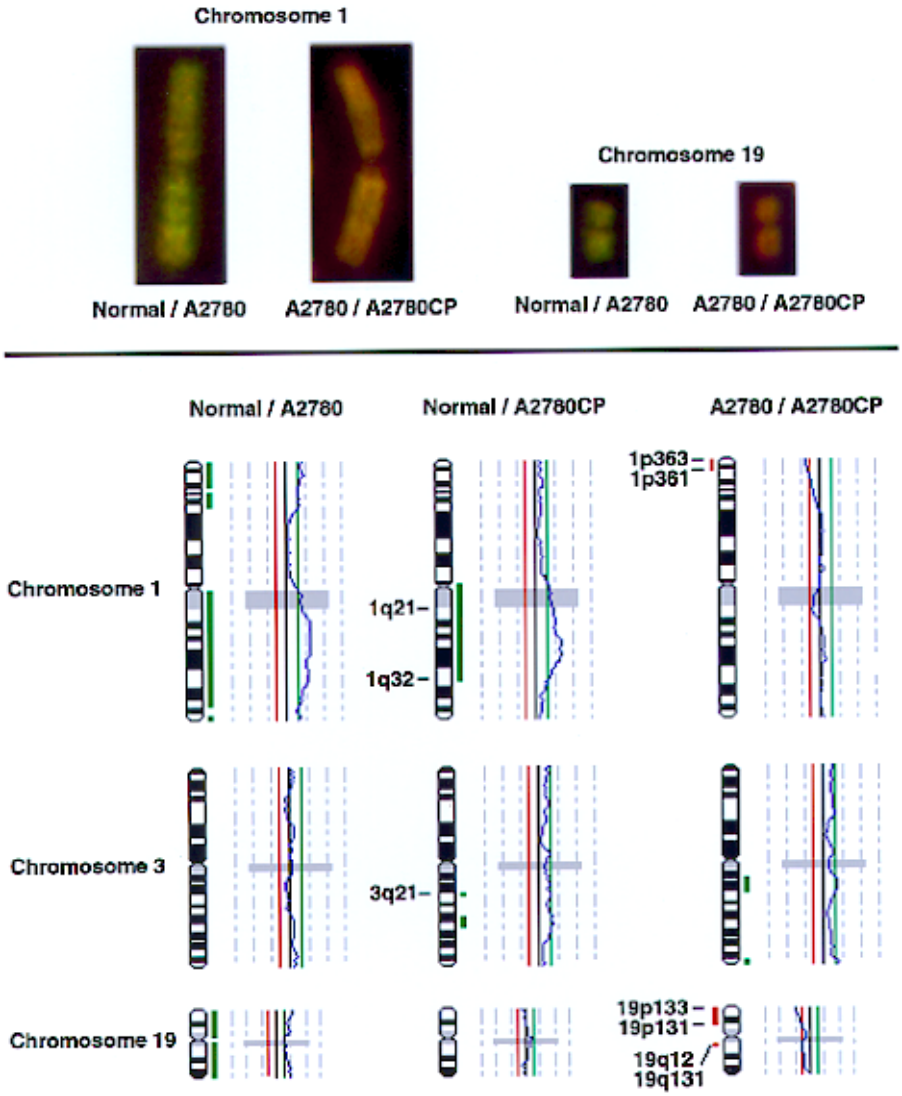

Fig. 2

Fig. 2 Representative fluorescence images and profiles showing gains and losses of DNA materials by CGH analysis.
(*Upper*) Hybridizations of fluorescence-labeled paired normal reference DNA (red) and DNA from A2780 cells (green), as well as paired DNAs from A2780 cells (red) and A2780CP cells (green) to chromosome 1 (left) and chromosome 19 (right) are shown.
(*Lower*) Intensity profiles of the mean red/green fluorescence ratios of each paired DNA sample in chromosome 1, 3, and 19 obtained from 5 metaphase spreads in each case. Green and red bars besides the chromosome regions indicate gains and losses of DNA materials at those regions. Central vertical line in the profile: baseline ratio value; green and red vertical lines: thresholds for gains and losses; wave line: the resulting ratio; and gray horizontal bar: centromeric region, which is usually eliminated from analysis. In cisplatin-resistant cells (A2780CP), gains of 1q 21-32 and 3q-21, and losses of 1p361–363, 19p131–133, and 19q12–131 were detected. These findings imply that specific genetic changes at these chromosomal regions may be involved in the development of resistance to cisplatin by ovarian carcinoma cells.

解説：癌治療薬であるシスプラチン抵抗性の卵巣癌培養細胞 A2780CP 株と，その親株である A2780 株を用い CGH 解析を行った．その結果，A2780CP 株は親株に対して 1p361–363，19p131–133 および 19q12–131 の欠損，そして 3q-21 の増幅を示した．これらの領域における DNA コピー数の変化が，卵巣癌培養細胞のシスプラチンに対する抵抗性獲得に関与していると考えられる．

References

Kallioniemi A, et al：Comparative genomic hybridization for molecular cytogenetic analysis of solid tumors. Science 1992; 258: 818—821.