[CANCER RESEARCH 58, 892–895, March 1, 1998]

Advances in Brief

Distinct Chromosomal Imbalances in Uterine Serous and Endometrioid Carcinomas[1]

Heini Pere, Johanna Tapper, Torsten Wahlström, Sakari Knuutila, and Ralf Butzow[2]

Department of Obstetrics and Gynecology [H. P., J. T., T. W., R. B.], and Laboratory of Medical Genetics [S. K.], Helsinki University Central Hospital, 00290 Helsinki, Finland

Abstract

Endometrial carcinoma shows various histological types that differ in their clinical presentation and prognosis. Comparative genomic hybridization was used to detect gains and losses of DNA sequences along all chromosome arms in 24 uterine serous and 24 uterine endometrioid carcinomas. In serous carcinomas, extensive genetic aberrations were detected in 17 of the 24 specimens, with a mean of 5.7 changes per tumor. The most frequent gains occurred at 3q (50%), 8q (33%), 5p (29%), 6p (29%), and 1q (29%), and the most common losses were located at 4q (17%), 15q (17%), and 18q (17%). Tumors exhibiting DNA copy number changes were associated with shorter overall survival. In endometrioid carcinomas, genetic aberrations were less frequent and simpler than in serous carcinomas. DNA sequence copy number changes were observed in 12 of the 24 cases, with a mean of 1.5 changes per tumor. The most frequent aberrations were gains at 1q (29%), 2q (13%), and 8q (13%). Losses were rarely observed. The diverging pattern of genetic changes observed in uterine serous and endometrioid carcinomas suggests different pathways of carcinogenesis in these tumor types.

Introduction

Endometrial carcinoma, the most common malignancy of the female genital tract, shows various histological types. The most common types are endometrioid and serous carcinoma, representing approximately 80 and 10% of all endometrial carcinomas, respectively. These two types clearly differ in their clinical presentation and prognosis, corresponding well to type I (estrogen-dependent) and type II (estrogen-independent) endometrial tumors (1). Endometrioid carcinoma is a relatively indolent neoplasm that typically occurs in association with unopposed estrogenic stimulation and endometrial hyperplasia. In contrast, serous carcinoma occurs in an older age group frequently adjacent to atrophic endometrium and is not associated with hyperestrogenism. Because of their aggressive behavior, serous carcinomas result in a disproportionate number of endometrial cancer deaths (2).

There is some evidence of diverse pathways of endometrial tumorigenesis. Several investigators have shown a high rate (greater than 80%) of positive immunostaining and mutations of p53 in serous carcinoma and in its putative precursor lesion, endometrial intraepithelial carcinoma (3, 4). In contrast, defects of p53 have been noted in only 10–25% of high-grade endometrioid carcinomas and not in atypical hyperplasia, the supposed precursor of endometrioid carcinoma (3, 5).

We used CGH[3] to identify DNA sequence copy number changes in tumor specimens from 24 uterine endometrioid and 24 uterine serous carcinomas. The advantage of CGH is that it enables the examination of gains and losses of DNA sequences within the entire tumor genome (6). Our aims were (*a*) to find out whether the copy number karyotypes of these two histological types are similar or dissimilar, (*b*) to identify chromosomal regions involved in their carcinogenesis, and (*c*) to compare the copy number karyotypes with clinical outcome.

Materials and Methods

Tumor Specimens. The material consisted of 24 cases of endometrioid and 24 cases of serous uterine carcinomas treated at the Department of Obstetrics and Gynecology, Helsinki University Central Hospital. All of the cases were reviewed by one gynecological pathologist (T. W.) before any further analysis was performed. Endometrioid carcinomas were classified from grade 1 to grade 3 according to International Federation of Gynecologists and Obstetricians criteria. Because this grading system is not applicable to serous carcinomas, these tumors were divided into two groups (lower and higher grade; Tables 1 and 2). The samples in the endometrioid group were selected to match the surgical stage of the serous carcinomas. Hence, the stage and grade of the disease, mean age at diagnosis, and death rate of these patients were higher than in an unselected group of endometrioid tumors. Forty-six of the samples were paraffin-embedded blocks, and two samples (cases 411 and 427) were frozen tumor sections. The specimens were trimmed by cutting out the normal tissue. The samples were found to contain approximately 70% tumor cells on histological examination. DNA was extracted according to standard protocols.

CGH. The CGH protocol for directly fluorochrome-conjugated nucleotides was followed (7), with modifications as described previously in detail (8). One μg of tumor DNA and reference DNA extracted from the blood of a healthy female donor were used for hybridization. The tumor DNA was labeled with fluorescein-12-dUTP or fluorescein-12-dUTP and fluorescein-12-dCTP (DuPont, Boston, MA). The reference DNA was conjugated to Texas Red-5-dUTP or Texas Red-5-dUTP and Texas Red-5-dCTP (DuPont). Twenty μg of human Cot-1 DNA were used to block binding of repetitive DNA sequences. The slides were counterstained with 4′,6-diamidino-2-phenylindole for identification of the chromosomes.

The hybridizations were analyzed using an Olympus fluorescence microscope and an ISIS digital image analysis system (Metasystems GmbH, Altlussheim, Germany). Three-color images, green for tumor DNA, red for reference DNA, and blue for the chromosome counterstain were obtained of 10 metaphases per sample. The cutoff value for losses was 0.85 and for gains 1.17. If the profiles exceeded the cutoff value of 1.5, the region was considered highly amplified. Ninety-nine % confidence limits with 1% probability of error were used to confirm the interpretation. The cutoff values were taken from negative control experiments using differentially labeled normal DNAs hybridized against each other. In the negative controls, the profiles never exceeded the above limits. Tumor DNA with known copy number changes was used in positive control experiments. Reverse labeling CGH (9) was performed on three samples (cases 333, 376, and 377), which confirmed the alterations detected by the standard technique.

Statistical Analyses. Differences in the frequency of individual chromosomal changes between the two histological groups were tested by using Fisher's exact test (two-tailed *P*s). Differences in the total number of changes in the patient groups were tested by using the nonparametric Mann-Whitney *U* test. The product-limit method was used to construct survival curves. The statistical significance of association with survival was tested by using the Cox proportional hazards model.

Received 10/30/97; accepted 1/13/98.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

[1] Supported by grants from the Helsingin Sanomat Fund, the Cancer Foundation of Finland, and the Helsinki University Central Hospital Research Fund.

[2] To whom requests for reprints should be addressed, at Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Haartmaninkatu 2, FIN-00290 Helsinki, Finland. Phone: 358-(0)9-4714912; Fax:358-(0)9-4714801; E-mail: ralf.butzow@helsinki.fi.

[3] The abbreviation used is: CGH, comparative genomic hybridization.

Table 1 *Histopathological and clinical characteristics and CGH findings in 24 uterine serous carcinomas*

Case No.	Stage	Grade[a]	Copy number changes[b]
317	IIIc	LG	None
318	IIIb	LG	+5, +7, +13
319	IV	HG	+1q, +2p15–pter, +2q24–qter/2q31–33, +3q21–qter/3q24–26.3, −4q24–q26, −4q32–qter, +5p, +6p21.1–pter, +7q, +8q13–qter/8q21.2–qter, +12q, +14q21–qter, −18q, +20q/20q13.1–qter
321	IIIc	HG	+3q25–qter, +8q
322	Ic	LG	None
324	IIIc	LG	+1p13–q13, +2q, +3, +6pter–q15/6p, +7q, +11q14–q23, −15, +17q, +18p/18p11.2, −18q21–qter, +19q13.1
325	IIIc	LG	+2q31–q33, +3q24–qter, −4q24–q26, −4q31.2–qter, +5p, −10q, +11q13–q21, −11q23–qter, +13, −15q24–qter
326	Ib	HG	+3q22–qter, +5p14–pter, −5q15–qter, +6p21.3–pter, −6q15–qter, −7p13–pter, −7q21–qter, −8p, +8q, −18
328	IIIa	HG	−4q13–qter, −6q13–qter, +8q, −9, +10p, −11p12–pter, +15/15q25–qter
330	Ic	HG	None
332	IVa	LG	None
333	IVb	LG	+8q21.2–qter, +19q
353	II	HG	+1q, +3q, −Xp, +6p21.1–pter, +8qcen–q23, −15qcen–q15
372	Ib	LG	None
373	IV	LG	+1, +2p21–p23, +2q13–q32/2q24–31, +3q13.3–qter, +5q23–qter, −11pter–q12, +11q14–qter, +13q14–qter, +17q24–qter, +20q12–qter
374	III	HG	+3q26.1–qter, −4p14–pter, −15q13–q21, +20q11–q13.2
375	IIIc	LG	None
376	IIIa	LG	+3q13.2–qter, +7p13–p21, +8q21.3–qter, +19q13.1–q13.2
377	IIb	LG	+1q41–qter, +2q33–q36, +3q21–qter, +5pcen–p15.1, +6p21.1–p23, +8p21–p22, −9p21–pter, +10q22–q25, +11p12–pter, +12p12–p13, +17q21–q25, +18pter–q12/18q11.2–12, −18q22–qter, +19, +20q
380	II	HG	None
381	IV	LG	+1q31–q32, +2q22–qter, +3q, +4pter–q24, +5q13–pter, −X, +6p12–pter, +7q21–q31, −8p12–pter, +8q12–q13, +8q22–qter/8q22–24.1, +11q, +12pter–q12, −15, −16q, +18q21–qter, +19q13.1, +20p
383	IIIc	LG	+1p22–p34.2, +2p22–q13, +3q25–qter, −4p, −4q32–qter, +5pcen–p14, +5q31–qter, −Xq, +6p21.1–p22, +7p13–pter, +7q21–q31, −9p21–pter, +10q22–q24, +11q12–q14, +12p, +12q14–q15, −13, +15q21–q24
411	Ic	HG	+12
427	Ic	LG	+1q31–q41

[a] LG, lower grade; HG, higher grade.
[b] +, gains; −, losses. High-level amplifications are underlined.

Results

Uterine Serous Carcinoma. DNA sequence copy number changes were detected in 17 of the 24 serous tumors (mean, 5.7 aberrations/tumor; range, 0–18; Table 1). Gains were more frequent than losses (2.8:1).

The most common region of relatively increased copy number, found in 12 cases (50%), was 3q, with minimal common region 3q26.1–qter. The gain at 3q was associated with a high number of genetic changes. When the samples with normal karyotypes were excluded, the mean number of changes per tumor with a gain at 3q was 10.2, and without the gain it was 1.1 ($P = 0.0095$). In eight cases (33%), the gains involved 8q, with minimal common region 8q23. There was no association between a gain at 8q and the number of genomic imbalances. Other common regions of gain (29%) were 1q, 5p, and 6p. High-level amplifications were found in six tumors (one to four regions/sample). Minimal common regions for the most frequent losses (17%) were 4q32–qter, 15qcen–q15, and 18q22–qter (Fig. 1).

In stage I–II and stage III–IV serous carcinomas, the mean numbers

Table 2 *Histopathological and clinical characteristics and CGH findings in 24 uterine endometrioid carcinomas*

Case No.	Stage	Grade[a]	Copy number changes[b]
5	Ib	1	None
9	Ib	1	None
12	Ib	1	+1q22–qter, −5q11.2–q21, −13q14–q21, −14, +17q22–qter
13	I	1	None
15	I	1	+1q, +10p
17	Ib	1	None
351	Ib	2	+1q
354	III	3	None
355	IIIa	2	+2q24–q32, +8q13–qter, +12p11.2–q12, +14q23–q24, −15qcen–q15, −16qcen–q13
356	IV	2	+6p21.2–pter, +12q13–q22, −15qcen–q15
357	IVb	2	None
358	IVb	3	+1q24–q42, +2, +4p13–pter, +6p/6p21–23, +8q21.1–qter, +11p12–p14, +11q13–q22, +12q13–q21, −16q
359	IIIa	3	+8q21.3–qter
360	IIIa	3	None
361	III	3	−8p
362	IIIc	3	+1q, +3q24–qter, +5q14–qter
363	III	3	+2q24–q32, +3q24–qter, +10p12–pter, +13q21–q22
364	IIIa	3	None
365	III	1	None
366	IVb	1	+1q/1q31
367	IVb	2	+1q
368	IIIc	1	None
369	IV	1	None
370	IIIa	1	None

[a] LG, lower grade; HG, higher grade.
[b] +, gains; −, losses. High-level amplifications are underlined.

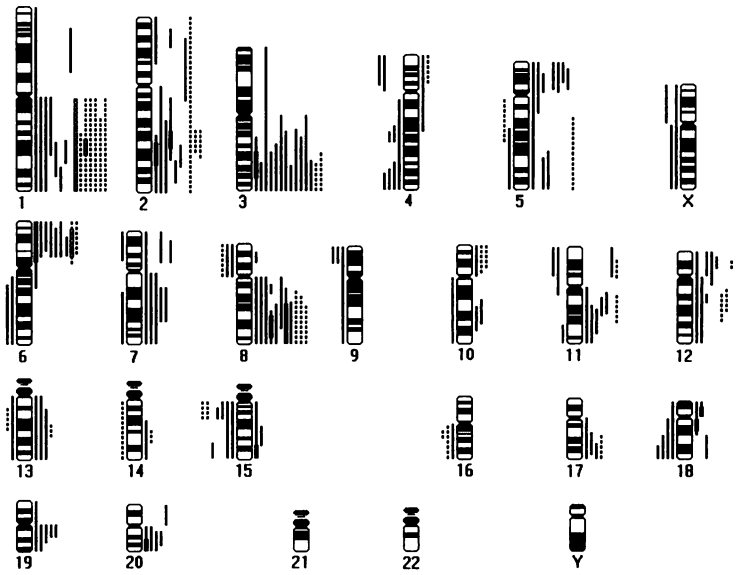

Fig. 1. Summary of gains and losses of DNA sequence copy number in 24 uterine serous and 24 uterine endometrioid carcinomas. Gains are shown on the *right*, and losses on the *left*, of the chromosomes. Each line represents genetic aberration seen in one tumor. ▬, high-level amplifications; ——, serous tumors; - - - -, endometrioid tumors.

of DNA copy number changes per sample were 3.7 and 6.9, respectively. Five of the six tumors exhibiting high-level amplifications were stage III or IV; one was stage IIb. When divided into two groups based on histological differentiation, the mean numbers of changes were 6.1 (lower grade) and 4.9 (higher grade).

Uterine Endometrioid Carcinoma. Copy number changes were found in 12 of the 24 endometrioid carcinomas (mean, 1.5 aberrations/tumor; range, 0–9; Table 2). Gains were more frequent than losses (3.6:1).

The most frequently gained chromosomal region was 1q, detected in seven cases (29%). Other common regions of increased copy number were 2q24–q31 (13%) and 8q (13%). High-level amplification was found in three cases (one region/sample). In total, there were only 8 regions of underrepresentation in 24 endometrioid carcinomas, and there was no specific pattern of distribution of these regions (Fig. 1).

In stage I–II and stage III–IV endometrioid carcinomas, the mean numbers of copy number changes per sample were 1.1 and 1.7, respectively. Comparing tumor grades, the mean numbers of changes were: 0.73 (grade 1), 2.2 (grade 2), and 2.3 (grade 3). The proportion of normal karyotypes detected by CGH was 72% in low-grade (grade 1) endometrioid carcinomas and 30% in high-grade (grades 2 and 3) carcinomas. High-level amplifications occurred in endometrioid tumors irrespective of tumor grade or stage.

Comparison of the Subtypes. Genetic aberrations were more frequent and more complex in serous than in endometrioid carcinomas; 71 *versus* 50% of cases showed copy number changes, with means of 5.7 *versus* 1.5 aberrations/tumor ($P = 0.014$). There were 10 highly amplified regions in the serous carcinomas compared with 3 in the endometrioid carcinomas.

The most frequent region of gain in serous carcinomas, 3q26.1–qter, found in 12 cases, was detected in only two endometrioid carcinomas ($P = 0.0034$). The gain at 5p (minimal common region 5p14), detected in seven serous tumors, was found in none of the endometrioid carcinomas ($P = 0.0094$). Overpresentation of 1q, 2q, 6p, and 8q was frequent in both types of endometrial carcinoma. The gains at 6p and 8q tended to be more common in serous than in endometrioid carcinomas, but these differences did not reach statistical significance.

Copy Number Changes *versus* Clinical Outcome. Of the seven cases of serous carcinoma with no copy number changes, five (71%) patients were alive and two (29%) had died, one of the disease and the other as a result of a surgical complication. In contrast, of 17 patients having tumors with copy number changes, 3 (18%) were alive (2 of them having only one change), and 14 (82%) had died of the disease. The mean follow-up times of live patients were 75 months (range, 21–142) and 34 months (range, 22–58), respectively (Fig. 2). The overall estimated hazard ratio for death in patients whose tumors had copy number changes detected by CGH was 10.8 ($P = 0.0059$) according to univariate analysis. When surgical stage was added to the analysis, neither stage nor number of changes was an independent prognostic factor. In endometrioid carcinoma, no association between copy number changes and survival was found.

Discussion

In our CGH study, we found that the two most common histological subtypes of endometrial carcinoma clearly differ in regard to their DNA sequence copy number karyotypes. The chromosomal imbalances were almost four times more frequent, and high-level amplifications were detected three times more often in serous than in endometrioid carcinoma. The patterns of copy number changes were also different in the two tumor types. In endometrioid carcinoma, the number of genomic imbalances paralleled the grade of the tumor, but in serous carcinoma, no such tendency was found, supporting the relevance of the grading system in endometrioid but not in serous carcinoma.

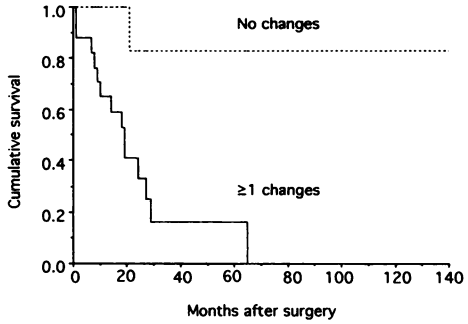

Fig. 2. Survival analysis of patients with uterine serous carcinoma according to DNA copy number changes detected by CGH. - - - -, no changes (1 of 6 died; the patient who died of a surgical complication was excluded from the analysis); —, one or more changes (14 of 17 died of the disease).

Serous and endometrioid carcinomas occur throughout the extended Müllerian system. Tumors of the same histological subtype also show similarities in clinical presentation (10). According to results of a CGH study of ovarian carcinoma, including mostly the serous subtype (11), and analysis of 37 cases of serous ovarian carcinoma,[4] the most common copy number changes detected are gains at 3q and 8q, resembling our results in uterine serous carcinoma. Furthermore, a gain at 1q was the most common copy number change detected in a study of eight endometrioid ovarian carcinomas, including high-level amplification of 1q in three cases (12). These data suggest a similar pathway of tumorigenesis in the same histological tumor types irrespective of the organ of origin in the female genital tract.

The most common copy number change in uterine serous carcinoma, a gain at 3q26.1–qter (including high-level amplification of 3q24–q26.3 in one case), has previously not been associated with endometrial carcinoma, which might be due to the small number of serous carcinomas included in previous studies. This area is of particular interest, because it has shown gain and amplification in several other malignancies, *e.g.,* carcinoma of the uterine cervix and squamous cell carcinoma of the lung (13, 14). There is no prominent oncogene mapped to this region, but several candidate oncogenes have been proposed, *e.g., EVI1* and *ECT2*. In our material, the gain at 3q was not found alone in any of the samples, and it was associated with a high number of genetic changes, suggesting a role in tumor progression rather than initiation. Another recurrent aberration in the serous subtype was a gain at 8q, including high-level amplification in two cases. Gain at 8q has also been reported in two serous carcinomas by Sonoda *et al.* (15). In our study, seven of eight gains involved 8q24.1, where the oncogene c-*myc* is located. However, we found that the minimal common region was located proximal to c-*myc*, suggesting the existence of another oncogene(s) at 8q23.

The most common copy number alteration in endometrioid carcinoma, a gain at 1q, included the whole chromosomal arm in five of seven cases and high-level amplification in two cases. There was no association between the gain at 1q and the number of genetic changes per tumor, and in three cases it was the only abnormality detected, suggesting that the gain at 1q could be an early event in this tumor type. Gain at 1q has been reported as the most frequent cytogenetic change in endometrial carcinoma (15–18), and it has also been found frequently in adenocarcinomas of other organs, *e.g.,* the breast (19). Several oncogenes are located in the long arm of chromosome 1, but the significance of these genes in the carcinogenesis of uterine endometrioid carcinoma remains unknown.

Losses were less frequent than gains in both histological types. In the endometrioid type in particular, they were rarely observed. In serous carcinoma, the most frequent regions of underrepresentation were 4q32–qter, 15qcen–q15, and 18q22–qter. In endometrial carcinoma, loss of heterozygosity has been found in several chromosomal regions, including 18q (20, 21). These studies mostly involved the endometrioid type, so the losses detected by CGH in serous carcinomas are novel findings, and these regions may harbor tumor suppressor genes relevant to this tumor type. One study on serous carcinomas revealed a high rate of loss of heterozygosity at 17p, where p53 is located (4). Interestingly, we found no copy number changes at 17p. This and the low frequency of losses detected in general might be due to deletions smaller than the resolution of CGH.

Uterine serous carcinoma has a very high rate of recurrence even in cases of apparently local disease, and survival does not correlate with grade. We found that patients with serous tumors exhibiting DNA copy number changes had a significantly shorter overall survival than patients with tumors lacking changes. No such association was found in endometrioid subtype. However, these samples were selected to match the serous carcinomas, so the prognostic value of CGH in an unselected material of endometrioid tumors remains unknown. Our findings suggest that in serous carcinoma, CGH could have prognostic significance.

We conclude that uterine serous and endometrioid carcinomas diverge with respect to their DNA copy number changes, suggesting different pathways of carcinogenesis. Several novel regions of the genome associated with the tumorigenesis of these tumor types were identified. Targeted molecular investigations of these regions may reveal genes of importance in the initiation and progression of uterine serous and endometrioid carcinoma.

[4] J. Tapper, S. Knuutilia, M. Seppälä, and R. Butzow, manuscript in preparation.

Acknowledgments

We thank A. Tenhunen and M. Forss for their help in collecting the material. The technical assistance of A. Ikonen and G. Arifdshan is gratefully acknowledged.

References

1. Deligdisch, L., and Holinka, C. F. Endometrial carcinoma: two diseases? Cancer Detect. Prev., *10:* 237–246, 1987.
2. Hendrickson, M., Ross, J., Eifel, P., Martinez, A., and Kempson, R. Uterine papillary serous carcinoma: a highly malignant form of endometrial adenocarcinoma. Am. J. Surg. Pathol., *6:* 93–108, 1982.
3. Sherman, M. E., Bur, M. E., and Kurman, R. J. p53 in endometrial cancer and its putative precursors: evidence for diverse pathways of tumorigenesis. Hum. Pathol., *26:* 1268–1274, 1995.
4. Tashiro, H., Isacson, C., Levine, R., Kurman, R. J., Cho, K. R., and Hedrick, L. *p53* gene mutations are common in uterine serous carcinoma and occur early in their pathogenesis. Am. J. Pathol., *150:* 177–185, 1997.
5. Kohler, M. F., Berchuck, A., Davidoff, A. M., Humphrey, P. A., Dodge, R. K., Iglehart, J. D., Soper, J. T., Clarke, P. D., Bast, R. J., and Marks, J. R. Overexpression and mutation of p53 in endometrial carcinoma. Cancer Res., *52:* 1622–1627, 1992.
6. Kallioniemi, A., Kallioniemi, O. P., Sudar, D., Rutovitz, D., Gray, J. W., Waldman, F., and Pinkel, D. Comparative genomic hybridization for molecular cytogenetic analysis of solid tumors. Science (Washington DC), *258:* 818–821, 1992.
7. Kallioniemi, O. P., Kallioniemi, A., Piper, J., Isola, J., Waldman, F. M., Gray, J. W., and Pinkel, D. Optimizing comparative genomic hybridization for analysis of DNA sequence copy number changes in solid tumors. Genes Chromosomes Cancer, *10:* 231–243, 1994.
8. El-Rifai, W., Larramendy, M. L., Björkqvist, A-M., Hemmer, S., and Knuutila, S. Optimization of comparative genomic hybridization using fluorochrome conjugated to dCTP and dUTP nucleotides. Lab. Invest., *77:* 699–700, 1997.
9. Larramendy, M. L., El-Rifai, W., and Knuutila, S. Comparison of fluorescein isothiosyanate- and Texas Red-conjugated nucleotides for direct labeling in comparative genomic hybridisation. Cytometry, in press, 1998.
10. Lauchlan, S. C. The secondary Mullerian system. Obstet. Gynecol. Surv., *27:* 133–146, 1972.
11. Iwabuchi, H., Sakamoto, M., Sakunaga, H., Ma, Y. Y., Carcangiu, M. L., Pinkel, D., Yang, F. T., and Gray, J. W. Genetic analysis of benign, low-grade, and high-grade ovarian tumors. Cancer Res., *55:* 6172–6180, 1995.
12. Tapper, J., Butzow, R., Wahlström, T., Seppälä, M., and Knuutila, S. Evidence for divergence of DNA copy number changes in serous, mucinous and endometrioid ovarian carcinomas. Br. J. Cancer, *75:* 1782–1787, 1997.
13. Heselmeyer, K., Schrock, E., du Manoir, S., Blegen, H., Shah, K., Steinbeck, R., Auer, G., and Ried, T. Gain of chromosome 3q defines the transition from severe dysplasia to invasive carcinoma of the uterine cervix. Proc. Natl. Acad. Sci. USA, *93:* 479–484, 1996.
14. Björkqvist, A-M., Husgavel-Pursiainen, K., Anttila, S., Karjalainen, A., Tammilehto, L., Mattson, K., Vainio, H., and Knuutila, S. DNA gains in 3q occur frequently in squamous cell carcinoma of the lung, but not in adenocarcinoma. Genes Chromosomes Cancer, in press, 1998.
15. Sonoda, G., du Manoir, S., Godwin, A. K., Bell, D. W., Liu, Z., Hogan, M., Yakushiji, M., and Testa, J. R. Detection of DNA gains and losses in primary endometrial carcinomas by comparative genomic hybridization. Genes Chromosomes Cancer, *18:* 115–125, 1997.
16. Milatovich, A., Heerema, N. A., and Palmer, C. G. Cytogenetic studies of endometrial malignancies. Cancer Genet. Cytogenet., *46:* 41–53, 1990.
17. Shah, N. K., Currie, J. L., Rosenshein, N., Campbell, J., Long, P., Abbas, F., and Griffin, C. A. Cytogenetic and FISH analysis of endometrial carcinoma. Cancer Genet. Cytogenet., *73:* 142–146, 1994.
18. Bardi, G., Pandis, N., Schousboe, K., Holund, B., and Heim, S. Near-diploid karyotypes with recurrent chromosome abnormalities characterize early-stage endometrial cancer. Cancer Genet. Cytogenet., *80:* 110–114, 1995.
19. Ried, T., Just, K. E., Holtgreve-Grez, H., du Manoir, S., Speicher, M. R., Schrock, E., Latham, C., Blegen, H., Zetterberg, A., Cremer, T., and Auer, G. Comparative genomic hybridization of formalin-fixed, paraffin-embedded breast tumors reveals different patterns of chromosomal gains and losses in fibroadenomas and diploid and aneuploid carcinomas. Cancer Res., *55:* 5415–5423, 1995.
20. Fujino, T., Risinger, J. I., Collins, N. K., Liu, F. S., Nishii, H., Takahashi, H., Westphal, E. M., Barrett, J. C., Sasaki, H., Kohler, M. F., Berchuck, A., and Boyd, J. Allelotype of endometrial carcinoma. Cancer Res., *54:* 4294–4298, 1994.
21. Peiffer, S. L., Herzog, T. J., Tribune, D. J., Mutch, D. G., Gersell, D. J., and Goodfellow, P. J. Allelic loss of sequences from the long arm of chromosome 10 and replication errors in endometrial cancers. Cancer Res., *55:* 1922–1926, 1995.

Distinct Chromosomal Imbalances in Uterine Serous and Endometrioid Carcinomas

Heini Pere, Johanna Tapper, Torsten Wahlström, et al.

Cancer Res 1998;58:892-895.