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SHORT COMMUNICATION

Chromosome 6q Involvement in Human Malignant Melanoma

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ABSTRACT: *Chromosome banding analysis was performed on five cases of human malignant melanoma. Results demonstrated a variety of chromosome alterations, including deletion or translocation of chromosome 6q, in four of five cases. A comparison of our results with previously published studies suggests that chromosome 6q may represent a specific site of chromosome aberration in malignant melanoma.*

A variety of tumor associated chromosome alterations have been described in hematopoietic malignancies (e.g., Philadelphia chromosome positive chronic myelogenous leukemia). However, relatively few have been described in human solid tumors (for review, see [1]). In our recent cytogenetic studies of human malignant melanoma, four of five patients demonstrated alterations of chromosome 6. In three patients a translocation involving the same chromosomal region 6(q15→23) was observed. A survey of the published literature further supports the common alteration of the long arm of chromosome 6 in this malignancy (Table 1).

G- and C-banding techniques [2] were utilized on all five samples analyzed in our study. Chromosomal banding analyses demonstrated a variety of clonal chromosomal abnormalities. Chromosomes involved in either numeric or structural alterations in at least four cases included No. 1, 2, 3, 6, and 7. The most common structurally altered chromosomal locus was region 6q15→23 (Fig. 1). Structural alterations of 6q observed included t(1;6)(q15;q23) (case MH), t(3;6)(p21;q23) (case RL), and t(6;?)(q21;?) (Case RW). A further case (SU) contained monosomy for chromosome 6 in all cells observed. Review of the very limited literature on human malignant melanoma studied by chromosome banding analysis revealed an additional nine cases containing chromosomal alterations of chromosome 6q (Table 1).

Recently we described an apparently tumor-associated cytogenetic alteration in tumor colony forming cells (TCFUs) from patients with human ovarian adenocarcinoma—the simple deletion of chromosome 6(q15→21) [3]. The deletion of 6q or

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Table 1 Alteration of chromosome 6q in banded cases of human malignant melanoma

Case no.	ID	Breakpoint origin	% of cells with 6q	Reference
1	RL	6q23	67	This report
2	RW	6q21	80	This report
3	MH	6q23	100	This report
4	CS	6q21	100	[11]
5	RJ_{1-5}[a, b]	6q2?	85	[12]
6	Colo 251[a]	6q21	ND[c]	[13]
7	Colo 239[a]	6q15	ND	[13]
8	Colo 299[a]	6q14	ND	[13]
9	Colo 297[a]	6q11	50	[14]
10	Colo 324[a]	6q21	50	[14]
11	Colo 381[a]	6q27	50	[14]
12	MM 138[a]	6q12	50	[15]

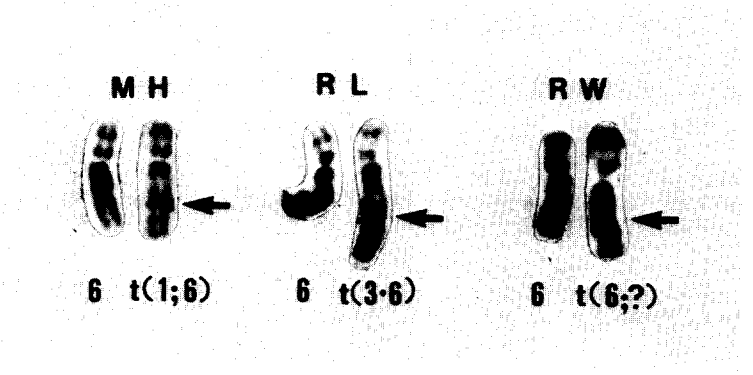
[a]Analysis performed on established cell line

[b]Five different cell lines were established from multiple metastases of this patient. All five cell lines contained the 6q marker chromosome.

[b]ND = Not determined by author.

its translocation in ovarian cancers has also been reported for ovarian serous cystadenocarcinoma by other groups utilizing nonclonal assays [4, 5]. The chromosome 6 alterations we have observed in malignant melanoma have involved the same chromosomal region we find frequently involved in ovarian adenocarcinoma. However, it must be stressed that not all ovarian tumors or melanomas display alterations of 6q [6, 7]. Furthermore, alterations of chromosome 6q have also been observed in various solid tumors (e.g., lung, cervix, and testicular cancers), as well as several hematopoietic malignancies (e.g., acute and chronic myelogenous leukemia) [8]. The current data related to chromosome 6q alterations suggest to us that this alteration may not be "specific" for either melanoma or ovarian cancer. Instead, the common occurence of chromosome 6q alterations in both of these malignancies, as well as in a variety of other cancers, appears to suggest a more general role for this chromosomal region in human cancer.

Figure 1 Evidence of chromosome 6q involvement in human malignant melanoma. Normal chromosome #6 is paired with the translocation marker (arrows). MH = t(1;6)(q15;23); RL = t(3;6)(p21;q23); and RW = t(6;?)(q21;?).



Unlike hematopoietic malignancies which often contain only a single clonal chromosomal alteration, human solid tumors ordinarily contain a variety of cytogenetic alterations [3, 8]. Thus, the biological consequences of an alteration of 6q, coupled to substantial aneuploidy within the genome, is currently indeterminate. Genes mapped to the area of 6q15→23 include phosphoglucomutase-3 (q21→qter), superoxide dismutase (mitochondrial) (q21), and malic enzyme (soluble) (q21→15) [9]. If future studies confirm region q15→23 of chromosome 6 as a very frequent site of chromosomal alteration in human malignancies, it may represent a region analogous to "hot spots" of chromosome breakage found in certain human hematopoietic malignancies [10]. Studies of the breakpoint regions of chromosome 6q by recombinant DNA techniques may provide important information on the molecular basis (e.g., *onc* gene sequences) responsible for this chromosome defect.

ADDENDUM

Following the acceptance of this manuscript, direct concordance between the chromosome location of the cellular oncogene c-myb and the breakpoints we have observed in malignant melanoma (6q15→23), has been reported (Harper, M. E., Simon, M. I., Franchini, G., Gallo, R. C., Wong–Staal, F., Proc. Natl. Acad. Sci., in press, 1983). This finding further supports the link between the chromosomal location of human oncogenes and tumor specific chromosome aberrations.

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