Chromosomal Heterogeneity in the RAG and MSWBS Mouse Tumor Cell Lines

Shahnaz Hashmi, Penelope W. Allderdice, George Klein, and Orlando J. Miller


SUMMARY

By means of a Q-banding technique, virtually every chromosome in two heteroploid mouse cell lines, RAG and MSWBS, has been identified. The origin of 60 to 80% of the chromosomes has been established; the remaining chromosomes can be identified as markers characteristic of the cell line.

The extent of chromosome heterogeneity has been examined and compared in these two mouse tumor cell lines. Each line is remarkably heterogeneous and, even within a line, cells with the same total chromosome number have karyotypes that differ considerably. There are distinctive differences in the chromosomal makeup of the two lines.

INTRODUCTION

The chromosomal and phenotypic characteristics of malignant cells have been widely studied for a better understanding of the factors involved in the initiation and progression or evolution of cancer. Furthermore, since many transplantable animal tumors retain their ability to elaborate, both in vivo and in cell culture, specialized products characteristic of the tissue of origin, they have been used to provide clues to the control of gene expression in differentiated cells.

Malignant cell populations, especially those growing in vitro, are frequently heteroploid, with marked numerical and structural variation in chromosome constitution (10) from cell to cell. Because of technical limitations in the identification of specific chromosomes by traditional cytological methods, the use of malignant cell lines with restricted chromosome variability has many advantages.

Mouse cell lines MSWBS and RAG were chosen for this study because they were reported to be rather more homogeneous than many malignant cell lines. The MSWBS line is a variant of the MSWB sarcoma that was induced by methylcholanthrene in a male F1 hybrid between mouse strains A and A.SW (14). The MSWBS line was adapted for growth as an ascites tumor in the A.SW parent and expresses only the H-2a not the H-2k histocompatibility complex. The MSWBS line has been used in immunological studies designed to explain the mechanism of suppression of histocompatibility genes (15) and in the genetic analysis of cancer (9).

The RAG line is a nonreverting 8-azaguanine-resistant line that arose from a spontaneous renal adenocarcinoma in a BALB/cd mouse of unspecified sex. It still expresses specialized functions such as the production of the kidney-associated esterase ES-2 (13). This line has been extensively used in somatic cell hybridization experiments, especially those designed for mapping human chromosomes and detecting linkage (2, 24).

Chromosome-banding techniques enable one to identify chromosomes with far greater accuracy than was possible with traditional staining techniques (23). Here we report the results of such a study of the MSWBS and RAG lines. This study has revealed unexpectedly great heterogeneity within each line and distinctive differences between these 2 lines; each has its characteristic chromosomal features and pathway of evolution of the karyotype.

MATERIALS AND METHODS

RAG cells were grown as monolayers in Dulbecco-Vogt medium plus 10% fetal calf serum. Metaphase chromosome preparations were made by shaking exponentially growing cultures and collecting the detached mitotic cells. MSWBS cells were harvested directly from in vivo growth in an A.SW mouse. The subsequent steps leading to fluorescent karyotypes have been described in an earlier report (22).

Each normal telocentric chromosome was designated by its number (1 to 19 or X) according to the standard system (4). Chromosomes 9 and 13, which are similar in banding pattern, were considered as a group. Each unknown telocentric was designated as a marker, M1-M28 in RAG and M1-M12 in MSWBS. The marker numbers are specific to each line, i.e., M1 in RAG cells is not the same chromosome as M1 in MSWBS or as M1 of the A9 cells described by Allderdice et al. (1). The biarmed chromosomes in which both arms were of known origin were designated by numbers indicating the origin of each arm, separated by an oblique slash, e.g., 10/15. The biarmed chromosomes in which one or both arms were not identical with any telocentric chromosome of known origin were designated by the number of the marker and the number of the known chromosome separated by a slash, e.g., M30/14...
or the number of the markers separated by a slash, e.g., M2/M10, respectively.

RESULTS

The RAG Cell Line. Karyotypes of 20 cells were prepared. Two of these are shown in Figs. 1 and 2. The number of chromosomes in each cell ranged from 51 to 66, with a mean of 61.3 and no sharp mode. The number of telocentric chromosomes ranged from 47 to 60 (mean, 56.5) and the number of biarmed chromosomes ranged from 3 to 8 (mean, 4.7). With the quinacrine fluorescent banding patterns, it was possible to identify every chromosome. Every member of the normal mouse complement except the Y was present. More than three-fourths of the chromosomes were members of the normal complement or identifiable derivatives of them. The remaining chromosomes had specific banding patterns by which they could be recognized, but their origin could not be ascertained (Table 1). Telocentric markers were quite common; 24 were scored altogether. There were 20 biarmed chromosomes, of which 5 were isochromosomes.

There was variation from cell to cell in the number of copies of a given chromosome and in the range of chromosomes present. The distribution of the number of copies per cell of each chromosome in the sample of 20 cells is shown in Table 2. The number of copies of Chromosome 1, for example, is 1 in 2 cells, 2 in 9 cells, 3 in 8 cells, and 4 in 1 cell. The number of copies of normal chromosomes ranged from 0 to 5 per cell, with Chromosome 17 having the highest modal number. A modal number of 3 copies per cell was observed for Chromosomes 2, 4, 5, 6, 9 + 13, 11, and 14. The biarmed chromosomes and the telocentric markers, on the other hand, were rarely present in more than a single copy, and many of them were seen in only 1 cell.

Each cell differed somewhat in its chromosome content from all other cells, although most of the chromosomes in any 2 cells were the same (Figs. 1 and 2). Sixty-four different chromosomes were present in the 20 RAG cells, although no more than 37 were seen in a single cell. An estimate of the heterogeneity in the RAG cell line was obtained by plotting the cumulative mean number of different chromosomes against the number of cells examined, as described earlier (1). That is, one plots the mean number of different chromosomes in 1 cell, in any 2 cells, any 3 cells, and so on. The slope of the resultant smooth heterogeneity curve (Chart 1) indicates that about 6 additional marker chromosomes would probably have been found if 5 more cells had been examined. Variability between cells is also seen in the form of differences in the number of copies of specific chromosomes in each cell (Table 2). This table shows the range of variation of each chromosome although, unlike the heterogeneity curve, it does not have any predictive value.

Since more than three-fourths of the chromosomes could be related to the normal mouse genome, we were able to estimate the mean number of copies per cell of each mouse chromosome, whether in a telocentric or biarmed form (Chart 2). This varied from 1 copy of the X chromosome to about 4 copies of chromosome 15. A mean of at least 2 copies could be demonstrated for 16 chromosomes, and probably for Chromosomes 9 and 13, leaving only Chromosome 3 and X with fewer copies.

The MSWBS Cell Line. Karyotypes of 20 cells were prepared. Two of these are shown in Figs. 3 and 4. The number of chromosomes in each cell varied from 25 to 32, with a mean of 28.4 and modes at 28 and 29. The number of telocentric chromosomes varied from 16 to 21 (mean, 18.5) and the number of biarmed chromosomes varied from 8 to 11 (mean, 9.4). Virtually every chromosome could be identified by its quinacrine-fluorescent banding pattern.

Only 14 chromosomes of the normal mouse complement were seen. Chromosomes 2, 6, 17, and 18 each were only present as one arm of a biarmed chromosome. Chromosomes 4, 7, and Y were never present in an identifiable form. All other chromosomes were present, either as unchanged telocentric chromosomes or as components of biarmed chromosomes. Chromosome 17 was a component of 2 different biarmed chromosomes, both present in every cell. Biarmed chromosomes were common; 34 different ones were observed (Table 3). None of these were isochromosomes (in good preparations, the 9/9 is seen to be a 9/13 chromosome).

The variability in chromosome makeup of the cells in this line is illustrated in Figs. 3 and 4. Although these cells differ by only 1 in their total number of chromosomes (29 and 30), each contains 4 chromosomes that the other lacks, although some of the same chromosome elements are present in these four. Such differences account for the remarkable diversity of chromosomes seen in this line, 60, in only 20 cells, despite the small number of chromosomes per cell. The slope of the heterogeneity curve (Chart 1) enables us to predict that about 6 new marker chromosomes would probably have been found if an additional 5 cells had been examined.

Only about 60% of the chromosomes in MSWBS cells could be related to the normal mouse genome (Table 1). The mean number of copies per cell of each normal chromosome is

### Table 1

<table>
<thead>
<tr>
<th>Type of chromosome</th>
<th>RAG</th>
<th>MSWBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known origin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telocentric</td>
<td>78</td>
<td>46</td>
</tr>
<tr>
<td>Biarmed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identical arms (isochromosomes)</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Nonidentical arms</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Unknown origin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telocentric</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>Biarmed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identical arms (isochromosomes)</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Nonidentical arms</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Partially known origin Biarmed</td>
<td>3</td>
<td>14</td>
</tr>
</tbody>
</table>

Note the much higher proportion of telocentric chromosomes in the RAG cells and the high proportion of isochromosomes (absent in MSWBS cells) among the biarmed chromosomes of this cell line.
Table 2

Distribution of chromosomes in 20 cells of the RAG line

Note the greater variability in the number of copies per cell of the normal chromosomes than of structurally rearranged chromosomes.

<table>
<thead>
<tr>
<th>No. of copies per cell</th>
<th>Normal chromosomes</th>
<th>Structurally rearranged chromosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 2 3 4 5 6 7 8 9,13/2 10 11 12 14 15 16 17 18 19 X</td>
<td>19/2 19/3 10/8 15/10 14/11 11/12 15/12 16/14 12/15 10/10 12/12 15/15 18/18 M2/M2 M2/M10 M2/15 M30/14 M31/15 M32/18 M1 M2 M3 M4 M5 M6 M7 M8 M9 M10 M11 M12 M13 M14 M15 M16 M17 M18 M19 M20 M21 M22 M23 M24</td>
</tr>
<tr>
<td>0 1 2 3 4 5 6 7 8 9,13/2 10 11 12 14 15 16 17 18 19 X</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
<td>0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
</tr>
<tr>
<td>1 2 5 11 3 1 2 1 5 2 7 1 1 2 1 5 2 7 1 1 2 1 5 2 7</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
</tr>
<tr>
<td>2 9 8 7 4 13 6 2 10 4 10 4 4 9 2 10 2 3 1 2 3 4 5 6</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
</tr>
<tr>
<td>3 8 14 8 11 12 6 2 13 3 11 1 6 3 5 4 4 9</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
</tr>
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<td>1 1 1 1 1 1 1</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
</tr>
<tr>
<td>5</td>
<td>1 1 1 1 1 1</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
</tr>
</tbody>
</table>
shown in Chart 2. This ranged from 0 for Chromosomes 4 and 7 to slightly more than 2 for Chromosomes 10 and 19. Only 8 or 9 chromosomes were present in nearly 2 copies per cell, and 9 chromosomes averaged no more than about 1 copy per cell.

Comparison of the RAG and MSWBS Line. Each of these cell lines had distinctive chromosomal characteristics, indicating a distinctive pathway of evolution of the karyotype in each line. Among the more striking differences between the 2 lines were the following: (a) The n.f. (fundamental number) of the hypodiploid MSWBS cells approximated the diploid mouse complement, whereas that of the hyperdiploid RAG cells approximated the tetraploid. (b) All the normal mouse chromosomes except the Y were seen in RAG cells, whereas only about two-thirds of them were present in MSWBS cells. (c) There was more variation in the frequency of normal chromosomes in the RAG than in the MSWBS cells (Tables 2 and 3). (d) The marker chromosomes were unique to each line; those seen in RAG cells were not present in MSWBS and vice versa. RAG cells had twice as many different telocentric markers (24 versus 12) as the MSWBS cells but had only about one-half as many different biarmed chromosomes (20 versus 34) as the MSWBS cells. However, isochromosomes were seen in most of the RAG cells but not in MSWBS.

DISCUSSION

The application of chromosome-banding techniques to the study of heteroploid cell lines represents a major advance in somatic cell genetics. With the much more limited conventional methods of chromosome staining, only gross changes in chromosome morphology were detectable. Therefore the emphasis in the past was on the number of chromosomes and the number of gross morphological classes of chromosomes, mainly biarmed and telocentric. The characteristic fluorescent banding pattern of each chromosome now enables us to identify individual members of the complement.

The present analysis of the chromosomes of mouse cell lines has revealed a much greater degree of chromosome heterogeneity, and of a different type, than was previously suspected (18). The findings of Levan et al. (18) on the chromosomes of MSWBS emphasized the limited variability in this line. For example, they reported the presence of 8 to 11 biarmed chromosomes per cell. By using quinacrine-fluorescent banding patterns as a means of distinguishing one chromosome from another, we have been able to show that the 8 to 11 biarmed chromosomes are made up of at least 32 different combinations of arms. Presumably, a similar range of diversity was present in the MSWBS cells analyzed by Levan et al. (18). This could easily account for many of the discrepancies they observed in comparing the distribution of length of chromosome arms in MSWBS cells and in normal mouse metaphase cells, since they pooled the measurements of chromosomes from different cells on the assumption that cells with the same number of chromosomes had approximately the same chromo-
Table 3

**Distribution of chromosomes in 20 cells of the MSWBS ascites sarcoma**

Note the relatively small degree of variability in the number of copies per cell of both the normal and structurally rearranged chromosomes.

<table>
<thead>
<tr>
<th>No. of copies per cell</th>
<th>Normal chromosomes</th>
<th>Structurally rearranged chromosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 2 3 4 5 6 7 8 9,13 10 11 12 14 15 16 17 18 19 X</td>
<td>17/1 6/2 10/2 18/2 11/5 9/6 16/6 18/6 9/8 13/9 19/9 16/10 18/10 19/16 M13/1 M10/2 M6/6</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>3 18 19 5 1 18 15 19 19 19 6 19 3 19 19 19 3 10</td>
</tr>
<tr>
<td>1</td>
<td>17</td>
<td>2 1 15 18 2 5 1 1 14 1 17 1 1 1 17 9 1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

|                        | M6/9 M6/10 M15/11 M22/11 M9/16 M10/16 M2/17 M4/17 M4/19 M12/M6 M18/M12 M14/M13 M17/M13 M17/M16 | M1 M2 M3 M4 M5 M6 M7 M8 M9 M10 M11 M12 M13 M14 M23 |
| 0                      | 18 19 19 19 19 17 2 19 19 2 19 19 19 13 18 |
| 1                      | 2 1 1 1 3 17 1 1 18 1 1 1 7 2 |
| 2                      | 1                   |

|                        | M1 M2 M3 M4 M5 M6 M7 M8 M9 M10 M11 M12 M13 M14 M23 | 0 1 2 |
| 0                      | 4 5 15 18 18 12 18 11 17 19 3 1 19 19 19 |
| 1                      | 12 14 5 2 2 8 2 9 2 1 17 19 1 1 |
| 2                      | 4 1                   |

Note: The table presents the distribution of chromosomes in 20 cells of the MSWBS ascites sarcoma. The variability in the number of copies per cell is noted as relatively small for both the normal and structurally rearranged chromosomes.
some complement. The use of the quinacrine banding technique has clearly shown this assumption to be incorrect. Their conclusion, that the MSWBS line has undergone a large number of cryptotransformations, may still be true, but the number of such changes must be less than their measurements implied, since nearly one-half the biarmed chromosomes seen in this line appear to have been produced by centric fusion of 2 otherwise structurally normal chromosomes, and two-thirds of the remaining biarmed chromosomes contain an otherwise structurally unmodified chromosome as 1 arm. It is thus clear that chromosome measurements have limited utility and are potentially quite misleading in analyzing heteroploid comple-
ments unless used in conjunction with a banding technique for chromosome identification.

The RAG cell line also has a much greater degree of chromosome heterogeneity than was suspected on the basis of studies that emphasized total chromosome number and gross morphological characteristics (3). The use of a banding technique to identify individual chromosomes of this cell line reveals the presence of a wide range of chromosome variability. In fact, each cell in the sample of RAG cells we studied was unique in its chromosome content.

Banding analysis of the chromosomes of RAG and MSWBS cell lines has shown a large number of structurally rearranged chromosomes, of unknown or only partially known origin. Such chromosomes make up 16 and 36% of the average RAG and MSWBS cell complement, respectively. The cell-to-cell variation in these markers is so great that even the examination of reasonably large samples of cells would not guarantee that all the kinds present in each line could be seen; it is quite likely, in fact, that new markers are being created all the time. If so, cloning might reduce the heterogeneity in such lines to only a limited extent. In view of their heterogeneity, the RAG and MSWBS cell lines are not well suited as parental lines of interspecific somatic cell hybrids when cytogenetic studies are to be carried out.

Somatic cell hybrids have proved to be an extremely useful tool in revealing and explaining both fundamental and complex characteristics of mammalian cells. First, interspecific hybrids have been particularly useful in mapping human chromosomes by correlating the phenotypic expression of genes with the presence or absence of specific chromosomes. Characterization of the marker chromosomes in the parental cell lines of these hybrids with chromosome-banding tech-
niques is both useful and desirable, since translocations between the chromosomes of the 2 species have been reported (2). Second, somatic cell hybrids have been used to shed light on the genetic aspects of cancer in both man and mouse (9, 26). Harris et al. (9) have reported a suppression of cancer in some mouse-mouse hybrids, produced by crossing malignant and nonmalignant cells, with subsequent reversion to cancer associated with a loss of chromosomes from the hybrid cells. Now that each chromosome can be identified by the use of banding techniques, perhaps the critical chromosomes involved in the regulation of malignant growth can be determined. Similarly, Yoshida (26) observed a loss of malignancy in man-mouse hybrids, of which only the human parent was tumorigenic. This was also found to be associated with the loss of chromosomes, but in this case of human origin; the identification of the chromosomes was dependent upon the use of a chromosome-banding technique.

These studies provide some evidence that chromosome loss is not responsible for loss of 1 of the 2 H-2 histocompatibility complexes in a loss variant, the MSWBS line. Mouse linkage Group IX, which carries the H-2 locus, has been shown to be on Chromosome 17 (5, 22). The chromosome-banding studies on MSWBS cells indicate that each cell has 2 copies of Chromosome 17, each carried as 1 arm of different biarmed chromosomes. Since loss of 1 parental Chromosome 17 is thus unlikely, another explanation for the loss of histocompatability antigens must be sought, e.g., some epigenetic change, genetic recombination by somatic crossing over, or mutation.

The extensive chromosome heterogeneity of heteroploid cell lines has implications for studies of mutation rates. Methods have been developed for determining mutation rates in diploid organisms. These methods have sometimes been applied to heteroploid cell systems without due consideration for the possible sources of error that could arise in such cell populations. The mutation rates at specific gene loci, calculated on the basis of the expression of an altered phenotype in heteroploid cells, may not be very accurate because of the presence of a variable number of copies of normal chromosomes revealed by banding analysis. The presence of cells in which the allele in question is present in a monosomic or polysonic state would give an inaccurate mutation rate for that locus. Other workers (11) have pointed out that the high degree of chromosomal instability and polyploid characteristics of some heteroploid cell lines, e.g., HeLa S3, renders them disadvantageous for such genetic experiments. Consequently, attention was turned to Chinese hamster cells growing in vitro, again presuming that since the modal number of chromosomes is diploid there is relative homogeneity. The findings of Kato and Yoshida (12), who used banding analysis on Chinese hamster lines, make this assumption questionable.

The accurate identification of chromosomes made possible by banding techniques also has implications for the stem cell concept and the patterns of proliferation and growth of cell lines. For a long time, it has been thought that during the growth of a malignant line in vitro some cells are best adapted for the environmental conditions in culture and are responsible for the propagation of the cell line. This hypothesis, advanced by Makino (20), was called the "stem-cell concept." Its basis was the presence of a relatively consistent total chromosome number in a majority of cells, (called stem cells) of a number of rat tumors. This concept was supported by work on mouse tumors (19) and, again, the most reliable criterion of the stem cell was the chromosome number. Our evidence is that there is no stem cell karyotype in either the RAG or MSWBS cell line, although the latter has a sharp modal number of chromosomes. Such evidence arouses some suspicion with regard to the homogeneity of the stem cell lineage, in at least some tumors and cell lines.

Chromosome-banding techniques provide a means of obtaining far more detailed and reliable information about the evolution of the karyotype in cell lines. They have revealed a preponderance of certain types of chromosomes, e.g., iso-
chromosomes, in one line and their consistent absence in
another. In the RAG cell line, most biarmed markers are isochromosomes. Similar findings have been reported for the A9 cell line (1). In the A9 cells, as in cells of the RAG line, there are twice as many different isochromosomes as there are biarmed chromosomes with nonidentical arms. On the other hand, isochromosomes have probably not been seen in the MSWBS line, the apparent exception 9/9, being in reality a 9/13 translocation. Such variations among the biarmed group of chromosomes point toward different pathways and patterns of evolution in these cell lines.

What is responsible for the marked variation in the karyotype from cell to cell in heteroploid lines? Kraemer et al. (16) have claimed on the basis of fluorometric measurements of very large numbers of interphase and metaphase cells that the DNA content of the cells in various heteroploid lines is no more variable than that seen in diploid cell lines, and have suggested that there is a constant amount of DNA in each G1 cell in a heteroploid line. They have explained this by postulating that, at certain stages in the cell cycle, all the chromosomes in a heteroploid cell fuse end to end, forming a continuous strand. These continuous chromosomes, as suggested by Dupraw (6), are divided into a variable number of individual pieces, each bearing a single functional kinetochore. The consistency and the nature of the banding patterns of marker chromosomes, as well as that of structurally normal chromosomes from cell to cell, provide no evidence in support of the hypothesis that the DNA can be chopped arbitrarily into chromosomes of variable size. This study and the evidence from previous chromosome-banding studies of heteroploid cell lines (8, 21, 25) clearly indicate the constant location of the centromere in these systems. There appears to be no reason to invoke any mechanism other than the classic ones (chromosome breakage and rejoining) to account for the observed aberrations.

Regardless of the mechanism by which chromosome changes are produced in many tumors and cell lines, the more important question at this point is whether any of these changes are necessary or sufficient to produce cancer. Some tumors have a highly variable chromosome makeup (15), whereas others are known to be of fairly stable diploid and pseudodiploid constitutions (7, 17). Efforts have been made in the past to relate changes in the chromosome complement of tumors with their malignant properties. The use of chromosome-banding techniques holds the promise of providing much more accurate characterization of any chromosome changes that are associated with neoplastic transformation and should lead to a much better understanding of the role of changes in malignancy.

ACKNOWLEDGMENTS

We should like to thank Dr. Frank Ruddle for providing us with the RAG cells.

REFERENCES

Hashmi, Allderdice, Klein, and Miller


Figs. 1 and 2. Quinacrine-fluorescent karyotypes of 2 RAG cells, showing the number of copies of specific chromosomes of both known and unknown origin and the presence of structurally rearranged (marker) chromosomes in the 2 cells. Note the underlying basic similarity in the types of chromosomes of the 2 cells despite the variability in the number of copies of specific chromosomes and the composition of marker chromosomes. Chromosome 9 refers to both Chromosomes 9 and 13.

Figs. 3 and 4. Quinacrine-fluorescent karyotypes of 2 MSWBS cells. The first 3 rows represent the chromosomes common to the 2 cells; however, note the variability in the number of copies of Chromosomes 8, 9, and 10. The chromosomes not common to the 2 cells are shown in the bottom row. Note the different centric fusion translocation involving Chromosomes 9 and 6 in this row.
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*Cancer Res* 1974;34:79-88.

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