マウス雑種細胞にみられた染色体細胞粉化と核断片について

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SHORT COMMUNICATION

A NOTE ON CHROMOSOME PULVERIZATION AND NUCLEAR FRAGMENTATION OBSERVED IN A SOMATIC MOUSE CELL HYBRID[1)]

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Although an extensive chromosome loss has been known to occur during prolonged passages of various mammalian somatic cell hybrids, the mechanism leading to the chromosomal loss remains obscure. The present report deals with the process of chromosome elimination in a mouse cell hybrid, which was accompanied with chromosome aberrations and certain nuclear changes.

An intraspecific somatic cell hybrid was produced between A9 and LM(TK$^-$)C1-1D (hereafter referred to as C1-1D) cell lines, which derived from an L line of mouse cells. A9 is deficient in inosinic acid pyrophospholylase (Littlefield 1964), while C1-1D lacks thymidine kinase (Kit *et al.* 1963). Hybrid cells were isolated from the mixtures of both cells, use being made of their selective advantage to grow in HAT medium containing hypoxathine, aminopterin and thymidine, according to the method of Littlefield (1964).

A9 cells were heteroploid showing 51-59 chromosomes with a mode at 53, of which 18-22 were biarmed. C1-1D cells had 45-55 chromosomes, 52 at mode, of which 7 to 10 were metacentric. The A9/C1-1D hybrid-cell population examined 10 days after fusion showed an approximate sum of the chromosome numbers of both parental cells. The average chromosome-number was 102, including 26 (25-32) biarmed chromosomes (Table 1). Samples after 1.5-month *in vitro* passages in HAT medium showed 71-121 chromosomes. From then, the distribution shifted to a lower range from 60 to 109, indicating a progressive fall in chromosome number during the first 3 months (Table 1).

It is of particular interest to note that certain proportions of metaphase plates in the latter two samples contained structural aberrations such as rings, fragments and pulverized chromosomes, while no such aberrations were observed in the first sample (Fig. 1 and Table 1). Further noticiable was that there were massive nuclear segmentation and fragmentation in the same slides prepared from both 1.5- and 3-month samples though most nuclei in the earliest sample were round and regular in shape. (Table 1 and Fig. 2).

The above results may indicate that the progressive chromosomal loss has taken

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Table 1. Distribution of chromosomes and frequency of chromosomal aberrations and altered nuclei in hybrid cells

Age of hybrid cells	Range of chromosome no. (range)	*Cells with			**Nuclei with	
		ring	fragment	pulverization	fragment	segment
10 days	99–125 (102)	0	0	0	0	0
1.5 months	71–121 (97)	2%	2%	6%	1.2%	0.7%
3 months	60–109 (91)	4%	4%	12%	13.5%	7.1%

* Based on 50 metaphases in each sample.
** Based on 1,000 interphase cells in each sample.

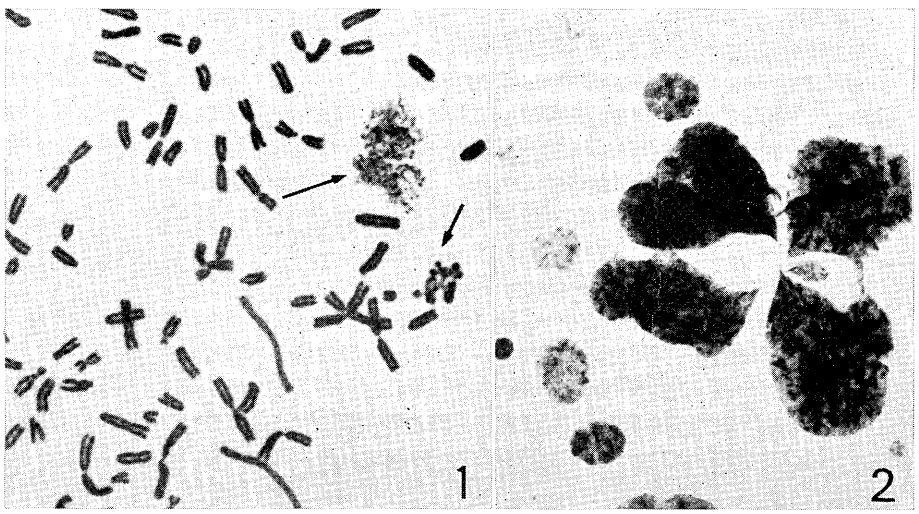

Fig. 1. Partial chromosome pulverization in an A9/C1-1D hybrid cell.
Fig. 2. Nuclear segmentation and fragmentation in an A9/C1-1D hybrid cell population.

place in parallel with the appearance of certain nuclear alterations and chromosomal abnormalities such as rings, fragments and pulverization. Engel *et al.* (1969) reported, in hybrid cells of a similar system, the frequent occurrence of nuclear polymorphism, together with unstable chromosome abnormalities with the passages of cultures. It seems that such nuclear and chromosomal structural changes may occur less frequently or more slowly under the ordinary culture condition as compared to those seen in the HAT system. Also conceivable is that such changes may occur more drastically in interspecific hybrids. For example, in human-Chinese hamster hybrid cells Kao and Puck (1970) observed very extensive and rapid loss of human chromosomes together with the appearance of pulverized and clustered chromosomes. Evidence has thus been accumulated that certain unstable changes of chromosomes and nuclear structure as well as the chromosome pulverization phenomenon may be causally related, at least in part, to the mechanism of chromosomal elimination in the hybrid system.

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