LACK OF SPONTANEOUS SISTER CHROMATID EXCHANGES IN SOMATIC CELLS OF *DROSOPHILA MELANOGASTER*—A REPLY

In a recent work (GATTI *et al.* 1979), we reported that sister-chromatid exchange (SCE) is not a spontaneous phenomenon in *Drosophila melanogaster*. Unlike in most animal and plant systems, where SCEs are more frequent than spontaneous chromosome aberrations by about two orders of magnitude, in *D. melanogaster* SCEs and aberrations occur at comparable rates. Therefore, SCEs, like chromosome aberrations, must be considered as cytological manifestations of errors occurring during DNA metabolism.

SCHONBERG argues that the lack of spontaneous SCEs in *D. melanogaster* is a necessity imposed by the somatic pairing of homologous chromosomes. He assumes that sister-chromatid exchange and mitotic recombination arise through the same molecular mechanisms. Thus, organisms such as *D. melanogaster*, in which homologous chromatids are strictly paired, would have evolved a low somatic recombinogenic activity in order to avoid mitotic recombination, which could lead to the homozygosity of deleterious genes. On the other hand, organisms such as mammals or plants lacking somatic pairing could tolerate relatively high somatic recombinogenic activities that would result in the production of some SCEs, but not in mitotic recombination.

A substantial similarity between the molecular mechanisms of sister-chromatid exchange and those of mitotic recombination has been recently suggested by KINSELLA and RADMAN (1979) to explain the processes of tumor promotion. They argued that the tumor promoter TPA induces enzymes involved in genetic recombination that would produce high frequencies of SCEs* and a parallel increase in the frequency of mitotic recombination. The mitotic segregation of recombinant chromatids would then produce cells in a "premalignant state" determined by the homozygosity of chromosome changes previously induced by "initiators" such as X rays or chemical mutagens.

The evidence for common molecular mechanisms underlying SCE formation and mitotic recombination is based upon two observations: (1) In Bloom's Syndrome, there is a dramatic increase in the frequency of spontaneous SCE and a concomitant high incidence of symmetrical exchanges involving homologous chromosomes at homologous sites; and (2) Mitomycin-C specifically induces sister-chromatid exchanges (LATT 1974) and symmetrical interchanges between homologous chromosomes (COHEN and SHAW 1964; SHAW and COHEN 1965; BRØGGER and JOHANSEN 1972). However, these observations are not easily interpretable because it is not clear how homologous chromatids, which in human cells are not normally close to each other, can interact in the formation of symmetrical interchanges (COMINGS 1975).

The best systems to investigate the relationships between SCEs and symmetrical interchanges, which are interpreted as cytological evidence for mitotic cross-

* LOVEDAY and LATT (1979) were not able to confirm that TPA induces high frequencies of SCEs.

ing over, are those with paired chromosomes throughout the cell cycle. These are: (1) endoreplicated cells in which sister chromosomes are closely paired to form diplochromosomes; and (2) cells with somatic pairing of homologous chromosomes.

The following observations gathered in these systems suggest that SCEs and symmetrical interchanges are not equivalent event at the molecular level: (1) In endoreduplicated cells, caffeine and cycloheximide significantly affect the frequency of SCEs and intradiplo-chromatid interchanges, but in different ways: caffeine reduces interchanges and increases SCEs; whereas, cycloheximide does not affect interchanges, but does suppress SCEs (SASAKI 1977). Moreover, PALITTI *et al.* (1977) found that there is not a parallel increase in SCE and intradiplo-symmetrical interchanges after treatment with X-rays, 4NQO and thiotepa. (2) In somatic cells of *D. melanogaster*, X-ray treatment during G2 induces high frequencies of symmetrical interchanges between homologous chromosomes (PIMPINELLI *et al.* 1976), but does not increase the frequency of SCE (unpublished observations). Conversely, treatments with low concentrations of Mitomycin-C greatly increase the frequency of SCEs, but do not substantially elevate the incidence of symmetrical interchanges (unpublished observations). (3) The meiotic mutants of *D. melanogaster*, *mei-9* and *mei-41*, which are severely defective in meiotic recombination, exhibit a parallel defect in the formation of symmetrical chromatid interchanges. Nevertheless, these mutants have almost normal levels of SCEs after treatment with 9μg/ml of 5-bromodeoxiuridine (GATTI, PIMPINELLI and BAKER 1980).

In conclusion, even though SCHONBERG's hypothesis is appealing, we feel that it should be considered with caution. Both SCEs and symmetrical chromatid interchanges do involve X-type physical exchanges of whole chromatids and might be expected to be generated by similar, if not identical, sequences of events; however, several observations suggest that some steps involved in the formation of SCEs do not participate in the formation of symmetrical interchanges.

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