日本人類遺伝学会第 29 回大会シンポジウム講演要旨

Abstracts of the Symposium, the 29th Annual Meeting of
the Japan Society of Human Genetics

Symposium I: Development of New Methods in Chromosome Study

Symposium I. Introductory Remarks by the Chairman

Kazuya MIKAMO

(Dept. Biol. Sci., Asahikawa Med. Coll., Asahikawa)

Since aneuploidy was first demonstrated to exist in humans twenty-five years ago, cytogenetics has made remarkable progress centering around human chromosome study. The sudden rapid progress that has been made in this direction was achieved owing to the application of new cytogenetic techniques to human cells. The new cytogenetic techniques have been devised one after another and followed by quick development, improvement and propagation. Thanks to these technical advances, the direct study of human chromosomes soon became an important part of medical research and helped to elucidate the causal mechanisms of a number of congenital anomalies whose etiology had long been unknown. In fact, the proofs shown in these studies have been definite and unequivocal because they were demonstrated as morphological changes clearly visible under the microscope. Recently, the high resolution banding method has made it possible to diagnose precisely even minute structural defects in chromosomes. Technical advance in this direction is further emphasized as it is predicted that there are a total of 2-3 thousand bands in human chromosomes.

Today, cytogenetic methods are developing variously and divergently owing to active adoption of knowledge and methods from biochemistry, molecular biology, biotechnology, *etc.*, all of which are rapidly developing in their own right. Therefore, it was a hard task for me to choose five topics for the symposium from such a field of amazingly great variety. The main purpose of this symposium is to discuss the inventions and discoveries recently made in connection with the methodology of direct chromosome study. I believe that the selected topics are fundamental, opening up new approaches to the investigation of not only chromosomal diseases, but also the biological nature of the chromosome and its properties. I am also sure that each speaker is at the frontier of a new field of chromosome study in which the advances yet to be made will be of great importance in the near future. The speakers will make it evident what direction these advances will take. It is my hope

that this symposium will be found interesting and instructive by all of the audience, whether they be geneticists or physicians.

S I-1. Sister Chromatid Exchange: Its Formation and Relations to Human Environment and Health Situations: Kanehisa MORIMOTO (Dept. Public Health, Univ. Tokyo, Tokyo)

Sister chromatid exchange (SCE) is a reciprocal exchange of DNA double strands contained in sister chromatids at apparently homologous sites. I will review available information as to the agents causing SCE and their categorization, and propose possible molecular mechanisms of SCE formation. I will also introduce the results in my recent study on possible correlations between SCE frequency in peripheral lymphocytes and ways of living (life style) and health situations in individuals who received a health examination at a health center in the Tokyo area.

In spite of intensive proposals of molecular mechanisms of SCE formation, there is no definite experimental evidence for the proposed mechanisms of SCE formation. It appears that SCEs take place through several different molecular processes, mainly depending on the types of causative damage. Recent studies have clearly shown that the many-fold higher frequency of baseline SCEs in cells from patients with Bloom's syndrome is due to their abnormal hypersensitivity to the incorporated BrdUrd. Because the baseline SCE frequencies are about the same in repair-deficient cells (except the cells from the patient with Bloom's syndrome) as in normal cells, it is likely that SCE formation is a surviving-rescue process from lethal and inappropriate cellular damage that is completely different from the known repair processes.

Many studies have shown that SCEs can be caused by DNA damaging agents, agents that cause conformational changes in chromatin structure, metabolic inhibitors such as DNA or protein synthesis inhibitors, hypo- and hyper-thermia *etc.*, besides their spontaneous occurrence. Tumor promoters have also been shown to cause SCEs. These agents are mutagenic and carcinogenic in many test systems. Thus SCEs are considered to be a good test system for detecting mutagens and carcinogens in the environment. In the recent surveillance on the correlations between *in vitro* SCE induction and mutagenicity and carcinogenicity, which I did as a member of the JETOC committee, it has been shown that the induction of SCEs has a good positive correlation with both mutagenicity (Ames test) and carcinogenicity (IARC) as with chromosomal aberrations. Since the SCE test is simpler in scoring than the chromosomal aberration test, the SCE test will be recommended in the future as a second screening method using mammalian and human cells.

The method of differential staining of sister chromatids is also used to distinguish between cells that have undergone different numbers of cell divisions in culture, and to investigate