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Aneuploidy as a Human Health Problem of Significance in Environmental Mutagenesis

The Workshop on Systems to Detect Induction of Aneuploidy by Environmental Mutagens was organized to fulfill several needs. The most pressing need is to provide a capability that can be used in screening programs involving tests on thousands of untested environmental chemicals. None of the assay systems currently proposed for use in these screening programs can detect chemicals producing aneuploidy by nondisjunction or any other mechanisms. It is essential to have the capability to detect those chemicals whose sole genetic effect may be the induction of aneuploidy as well as those chemicals which induce aneuploidy along with other types of genetic damage such as gene mutations and chromosome aberrations.

The differences between prokaryotic and eukaryotic organisms, with regard to chromosome structure (DNA versus nucleoprotein) and behavior during cell division, effectively limits assay system development to eukaryotes. Even among eukaryotes, differences in chromosome structure both with regard to histone and nonhistone proteins as well as the organization of the DNA (relative frequencies of repetitive versus nonrepetitive sequences) may confer a specificity that will make extrapolation from lower eukaryotes to higher eukaryotes difficult if not impossible. We do not know how serious these problems will be on the basis of present data, but because of the urgency of this problem, we must make a start towards test system development even in the absence of such knowledge.

In this workshop we have attempted to make a coordinated evaluation of these and related problems with regard both to the initial detection of chemicals which can cause aneuploidy, as well as, the additional assays that would be required for informed risk estimation. A review of the data in papers available in the open literature shows that relatively few assay systems have been developed with this genetic endpoint in mind, and that the number of chemicals which have been tested in those assay systems is quite limited.

In the strictest sense, this workshop is intended as a beginning in the process of stimulating research in a somewhat neglected area of environmental mutagenesis. There is little doubt in our mind concerning the necessity to limit human exposure to chemicals that would cause this type of genetic damage in the human population. Even in the absence of a comprehensive data base with regard to the incidence of various syndromes resulting from aneuploidy on a world-wide basis, the effects of aneuploidy in the human population are well known. Downs' syndrome, for example, is at a high enough frequency in our population that chance encounters are a relatively frequent occurrence, and this syndrome is only part of the total disease burden resulting from aneuploidy! In order to deal with this problem, the first step is to identify agents capable of inducing aneuploidy, and the second step is to limit human exposure to those agents that might increase frequencies of autosomal and related sex-chromosome anomalies in our population. This reduction in exposure would serve a dual purpose of (1) avoiding an induction of aneuploidy that would lead to an increase in the frequencies of these types of genetic diseases and (2) reducing the current incidence, if indeed, our "spontaneous frequencies" are the result of inadvertent exposure to active agents that are an already accepted part of our environment.

In this workshop there has been an attempt to explore the utility of various test systems that have already been developed for their suitability for use in mass-screen programs as well as to evaluate test systems in higher eukaryotes that can provide a data base more suitable for risk estimation. Finally, there

has been an assessment of those assay systems which have been proposed for use on man. It is only with these latter tests that we can evaluate directly the consequences of exposure to active chemicals both with regard to genetic damage in somatic cells and germ cells in high-risk worker populations or other groups on our population at high risk.

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