news and views

Information transfer in mammalian cells

from M. Bobrow and E. Solomon

IT is a long time since the discovery of bacterial transformation demonstrated that small amounts of foreign genetic information can be introduced into a living cell, and can function there. The explosive development of techniques for genetic and general biological experiments on eukaryotic cells in culture has led naturally to the search for an analogous system for the transfer of genetic information between cells of higher organisms.

Quite substantial progress has been made at several different levels, and it is now clear that the genetic information of complex organisms can be introduced into a foreign cell, and can function satisfactorily in this new environment. Whole nuclei can be introduced mechanically into the enucleated cytoplasm of another cell type (Gurdon, *Adv. Morphogenesis*, **4**, 1; 1964). Somatic cell hybrids, usually made with inactivated Sendai virus (Harris, *Cell Fusion*, Oxford University Press, 1970; Ephrussi, *Hybridization of Somatic Cells*, Princeton University Press, 1972), initially also produce two or more different functional nuclei within one cytoplasm, but this is followed by nuclear fusion resulting in mononucleate cells containing chromosomes of both parental types. In many situations, particularly where the cells used are from different species, these hybrids subsequently lose chromosomes of one parental type, leading eventually to cell lines which contain relatively few 'foreign' chromosomes within their nuclei. Chromosomes introduced in this way can express their genetic information, and this system has been extensively used for the formal genetic analysis of human chromosomes (*Rotterdam Conference*, The National Foundation, 1974), studies on regulation of gene expression and so on.

An extreme example of chromosomal segregation in hybrid cells is provided by situations in which an enzymatic function of one parental type is retained in the hybrid, but no corresponding chromosome can be detected in the karyotype (Schwartz *et al.*, *Nature new Biol.*, **230**, 5; 1971; Klinger and Shin, *Proc. natn. Acad. Sci. U.S.A.*, **71**, 1398; 1974). The probable explanation is that a chromosomal rearrangement has occurred, translocating a small segment of the donor genome into the host cell's karyotype. Thus, a microscopically undetectable amount of foreign genetic information is integrated, with some degree of stability, into the host cell genome.

Many workers have attempted to demonstrate the uptake of isolated chromosomes or purified DNA by eukaryotic cells. Only recently, however, have any persuasive examples of this type of phenomenon been described. McBride and Ozer (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 1258; 1973) incubated isolated Chinese hamster chromosomes with mouse fibroblasts deficient in the enzyme HPRT. The absence of this enzyme makes cells unable to grow in selective medium containing aminopterin. In such a medium, McBride and Ozer isolated cell lines which had acquired the hamster HPRT enzyme, thus correcting the genetic deficiency of the mouse cells. Similar results have been obtained on incubating mouse cells with isolated human chromosomes (Burch and McBride, *Proc. natn. Acad. Sci. U.S.A.*, **72**, 1797; 1975; Willecke and Ruddle, *Proc. natn. Acad. Sci. U.S.A.*, **72**, 1792; 1975).

The difficulty in experiments of this sort is to distinguish genuine transfer of genetic information from mutational or induced changes occurring in the host cells themselves. Most enzyme-deficient cell lines used in selective culture systems do have a low but detectable rate of spontaneous reversion to the enzyme-producing phenotype. Results such as those of McBride and Ozer are made credible by the great care taken in characterising the HPRT enzyme in the 'corrected' cells, by a variety of techniques, as being of donor and not of host origin.

In none of these cases was there any identifiable donor chromosome present in the karyotype of the derived cell lines. Some of these 'corrected' mouse cell lines are quite stable in culture, and are possibly again the result of small chromosomal rearrangements, with fragments of donor chromosome being inserted into the host karyotype. The size of fragment transferred must, in all these experiments, be pretty small (estimated as less than 1.5% of the human genome) as no donor enzymes have been detected in the resultant cell lines other than the one (HPRT) specifically selected for by the culture system. The reason for the integrated fragment being so small is not yet apparent. This unfortunately limits the use of the technique for genetic experiments other than those dealing with a selectable enzyme itself, or genes very closely linked to it. □

A hundred years ago

Oceanic Circulation

MR. CROLL'S statement (vol. xii, p.494), that the North Atlantic in lat. 38° is above the level of the equator, is based partly on the *Challenger* soundings and partly on Muncke's determinations of the thermal expansion of sea-water, which, however, *were not made on sea-water at all*, but on a saline solution prepared for him by Leopold Gmelin, according to data furnished by the incomplete analyses of Vogel and Bouillon La Grange. As Mr. Croll's statement depends on such very minute differences of volume, I am led to ask him to compare the rate of expansion of *real* sea-water, as determined by Prof. Hubbard, with Muncke's table; he will notice a discrepancy sufficiently wide to make it a matter of interest to ascertain how far the employment of the American observations may serve to substantiate or modify his conclusion.

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