The Washington Post

SUNDAY, MAY 28, 1967

Tumor Spread by Fusion

By Joshua Lederberg

Science and Man

SOMATIC HYBRIDIZATION of tissue cells has been the subject of previous comment in this column. We turn now to some recent findings having great interest in theoretical biology. They represent the work of several laboratories, notably Profs. Henry Harris of Oxford, Boris Ephrussi of Paris and Hilary Koprowski of the Wistar Institute, Philadelphia, and have been reported in the Proceedings of the Royal Society of London and of the National Academy of Sciences here.

A better demonstration of the evolutionary continuum cannot be imagined than that cells of fish, birds, mice and men can be mixed in any combination and chromosomes of each species will continue to function in the hybrid cells. The fundamental cellular processes of DNA-replication, its transcription into RNA and the coding by RNA of essential proteins are therefore compatible among these species—in fact, must be very nearly identical.

This is not to say that a normal developmental process leading to a whole organism could be expected from such combinations. Even within a species, this is too easily upset by minor quantitative changes in chromosome number. We can, however, begin to think of experiments in artificial evolution on the grandest scale, at least on a cellular level. It will be surprising if we fail to find cell hybrids between species as useful in medicine as animal and especially plant hybrids have been in agriculture.

SOME OF THE most interesting experiments are preliminary but cogent attacks on problems of tissue differentiation, cancer and virus biology. Cells of different tissue types can be fused, allowing rigorous questions to be asked concerning the mechanism whereby some cells behave as muscle, others as nerve and so on. The most favorable experimental material has quantitatively measurable products specific to the tissue.

For example, melanoma is a tumor characterized by the formation of dense pigment, a property maintained in tissue cultured from single cells. Hamster melanoma cells were hybridized with various cell lines of the mouse. The mouse-hamster combination is a favorable one since the chromosomes of the parent species are very different in size and shape and each can be recognized in the hybrid.

The hybrid cells all failed to make pigment. This illustrates an active suppression of this biochemical capability of the hamster chromosomes. It corroborates an important theoretical principle of embryology and opens the way to further critical experiments on the mechanism of that suppression—in particular, to explore the analogy with genetic repressors studied in microbes.

Similar results have been obtained with another highly differentiated tumor, the teratoma. This remarkable cell line has many of the potentialities for tissue organization possessed by the primitive embryo. It differs from the embryo mainly by its chaotic disorganization and its unlimited growth. Hybrids of teratoma cells with other kinds of cells are still tumorous but have suppressed many of their tissue potentialities.

On the other hand, other qualities of tumor cells, and especially their quality as tumors, are often retained in cell hybrids. This shows that the cancerogenic quality itself is a positive attribute of the cell, not, as some have thought, merely the loss of certain restraining genes.

Some specific cell substances are also retained in amounts proportional to the proportion of corresponding chromosomes when hybrid cells are formed. These functions are therefore controlled from within the chromosome, not by some diffuse suppressor in the cytoplasm.

Since cell fusion can also occur within the intact animal, the possibility is raised that tumor spread and some more mysterious changes in tumors might result from it. The fact that certain viruses and chemicals can promote cell fusion also opens new routes for subtle effects of these agents in provoking tumors and other diseases.