

Science and Man . . .

By Joshua Lederberg

Cell Biology

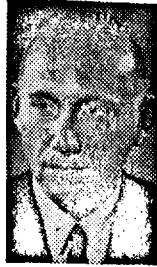
I HAD AN opportunity to hear an impromptu seminar by Dr. Hilary Koprowski, director of the Wistar Institute of Philadelphia, when I was in Pavia, Italy, recently.

He recounted his work on the cryptic stages of the life of certain viruses in cells of human or monkey origin. This was first reported in more preliminary form at scientific meetings in Atlantic City, N.J.

The virus that was the object of these studies is SV-40, discovered to be endemic in certain wild monkeys after it was revealed as a contaminant of polio vaccines. SV-40 has many fascinating properties, including its potentiality for inducing tumors when injected into newborn hamsters.

It is doubtful whether SV-40 plays an important role in human disease. However, it is an important experimental tool for fundamental studies of the way in which other viruses might work.

When cultured cells are freshly exposed to SV-40,



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many may be killed, but others are "transformed" into new varieties of cells. These are recognized by altered shapes, by the presence of new antigenic substances and above all by their malignancy when inoculated into susceptible animals.

Persistence of the infecting virus might be blamed for these changes. However, it has been possible to purify the transformed cell lines and cultivate them for years (a thousand cell generations) without any actual virus being any longer demonstrable.

Dr. Koprowski applied the technique of somatic cell fusion to this problem. He promptly found that SV-40 virus reappeared in every combination of transformed cells fused with sensitive ones. It should be stressed that no cell entering into the fusion showed virus. The same result was obtained with combinations of monkey and human cells, and by fusions of cells of the same species.

This extraordinary result is analogous to previously established findings on bacterial viruses. The analogy helps to support the orientation of future research, as well as some predictions that relate to its human significance. In both situations, the key to further progress is the development of new techniques and understanding of cell behavior.

The essential insight is that viruses can enter the genetic material of the cell and remain there in a cryptic form for an indefinite number of generations. Their presence is sometimes revealed by secondary effects on the cell, which may include malignant changes. Many generations later, the virus may reappear when some drastic change in cell chemistry occurs, as upon somatic hybridization with an uninfected cell. Related effects have been shown upon reinfection with an-

other virus. The conditions of its reappearance will be an important target for further research.

Since fusion can occur between cells of different species, the whole living world constitutes a potential reservoir of new viruses, some of which may have been cryptic since pre-human times.

The technique of cell fusion is now one of the most powerful methods for studying the role of cryptic viruses in human cancer. Perhaps even more important, in the long run, is the opportunity to alter the genetic material by the calculated use of viruses carefully studied for their specific effects.

Pavia is one of the oldest scientific universities in the world. Its ancient buildings now include a leading center of Italy's scientific renaissance in modern biology.

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