Speculations on Viruses, Cells and Evolution

Hyman Hartman
Department of Surgery
Children's Hospital Medical Center
300 Longwood Avenue
Boston, Massachusetts 02115

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ABSTRACT: Viruses are considered to be evolutionary agents. In bacteria, viruses are involved in recombination by infection. In eukaryotic cells, viruses are postulated to be involved in speciation and differentiation.

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Viruses have always been controversial as they seemed to bridge the gap between the living and the non-living world. "Viruses are submicroscopic entities that behave like dead inert matter unless placed in certain living cells. As parasites in these cells, however, they show the fundamental characteristics of life - self-duplication and mutation. On the other hand many viruses have the structure typical of inorganic matter; they are crystals. In size they range from the more complex protein molecules to the smaller bacteria. Chemically they consist of nucleoprotein, as the genes do. A virus is clearly something like a "naked gene (Weyl, 1949)". This is an historical statement made before the molecular biological revolution.

In its guise as a naked gene, the virus has certainly been the hero or heroine of molecular biology. This is not to say that any virus is merely a naked gene as it is a system of a number of genes. However, as was pointed out by one of the leading students of viruses, S. Luria, "the study of virus structure and multiplication always leads us back to the cell as the system in which the phenomena of life take place, so the problem of virus origin has led us back to the origin of the cell as an integrated whole. A virus is nothing but a part of the cell. We observe and recognize as viruses those parts independent enough to pass from cell to cell, and we compare them with other parts that are tied up with the whole system" (Luria, S.E. and Darnell, J.E., 1967).

The problem of the origin of viruses has recently led to two suggestions: 1) That the viruses are the result of progressive parasitic degeneration of micro-organisms (Green, 1935); 2) They have developed from the host's genome (Todaro and Hiebner, 1972).

Prokaryotic Viruses

In bacteria, since they are incapable of phagocytosis (Stanier, 1970), it is unlikely that viruses arose as a result of intracellular degeneration of a micro-organism. It is more likely that bacterial viruses originated from some components of the cell's genome.

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In bacteria an extensive system of recombination by infection has developed. Transformation, transduction, exchange of plasmids and episomes are all recombinational systems by infection. These systems have relegated sexual recombination to a comparatively minor role in the prokaryotes.

Virulent viruses are just the tip of the iceberg when one, "envisages viruses as primarily agents of gene exchange between cells" (Reanney, 1974).

Therefore when one considers evolution in prokaryotes, "it is no longer possible to draw a firm line of demarcation between chromosomal and cytoplasmic genetic determinants, between viral and non-viral elements, or even between viral and bacterial genes. All can merge into one another as a result of mutational and recombinational events" (Hayes, 1968).

Eukaryotic Cells

It is with the eukaryotic cells that the picture becomes more complicated. The difference between the highly differentiated eukaryotic cell and the less differentiated prokaryotic cell is a primary division between cell types. "It is now evident that the biological gap which separates bacteria and blue-green algae from all other cellular organisms represents one of the largest evolutionary discontinuities in the present day living world" (Stanier, Doudoroff and Adelberg, 1970).

Mereschkowsky (1905) developed a theory that envisaged the origin of the eukaryotic cell as a series of endosymbiotic events. He "developed the hypothesis that the dualism of the cell in respect to nuclear and cytoplasmic substance resulted from a symbiotic association of two types of primordial microorganisms, that were originally distinct, one including primitive non-nucleated monera composed of amoeboplasm, the other ultramicroscopic bacteria-like biococci. By ingestion of the latter by monera arose a symbiotic association of the two forms, the cocci becoming chromidial granules and thus ultimately forming the nucleus" (Wilson, 1925).

To the question, "How could the original membrane-bound nucleus have arisen"? Pickett-Heaps (1974) has suggested "that perhaps - like the chloroplast and mitochondria, it also arose as the result of a symbiosis, i.e. that an ingested organism somehow became the nucleus perhaps following the loss of much of its own cytoplasm".

If the nucleus, mitochondria and chloroplasts are the result of symbiosis, then the organism that did the ingesting did not have DNA.

Jeon and Danielli (1971) suggested, "that nuclei and DNA-containing bodies in general are also symbionts in cells that originally contained genetic RNA, and that DNA gradually took over the functions of such RNA, thereby permitting more sophistication of cellular mechanisms. In this case the genetic RNA, for which occasional evidence is seen, represents a survival of the pre-DNA cellular phase of evolution".

This would mean that the eukaryotic cell is basically a balance between an ancient RNA form of Amoeboplasm and a more modern and streamlined DNA-based prokaryote.

Eukaryotic Viruses

These considerations could explain why, "most of the viruses affecting differentiated (eukaryotic) organisms contain RNA. Almost all plant viruses contain RNA and, according to currently available evidence about 70% of known animal viruses contain RNA. By contrast, in prokaryotes, the vast majority of phages contain duplex DNA" (Reanney, 1974).

Since the vast majority of eukaryotic organisms use sexual means for recombination, the use of viruses for recombination by infection must be negligible.

Three considerations concerning viruses in eukaryotic organisms will be discussed in this paper.

1) Since endosymbionts are possible in the eukaryotic cell, some may have degenerated to the virulent viral stage. Therefore some viruses are degenerated micro-organisms (e.g. Vaccinia).

Differentiation

2) The RNA viruses may be used in the processes of embryonic differentiation and so one may have differentiation by infection. In recent years claims have been made concerning RNA transfers between macrophages and lymphocytes which underlie the production of antibodies. It has also been claimed that RNA extracts from lymphoid cells immunized *in vitro* can convert lymphoid cells from non-immunized animals *in vivo* and *in vitro* to antibody forming cells (Fishman and Adler, 1963). These processes are certainly differentiation by infection. In a recent symposium on, "RNA in the immune response", Haurowitz (1973), concluded, "that RNA plays a much more important role than most of us believe, not only in the production of the highly variable immunoglobulins but also in the process of differentiation in general". The problem of differentiation by infection will certainly have to await a full understanding of the molecular mechanisms underlying antibody formation.

Speciation

3) In a sexually recombining population, speciation becomes a problem. It was Goldschmidt who first postulated, "that scrambling and repatterning of the polarized sequences of chromosomal sections may occur occasionally in a single event, which I called "systemic mutations". Such repatternings in all grades, from small inversions or transpositions in one chromosome to a complete repatterning of all chromosomes may lead, if viable, to a large overall effect changing major features of development and producing in one step (or a few successive ones) a major evolutionary deviation. This hypothesis involves, of course, the idea that evolution, except on the lowest intraspecific level, proceeds by saltation rather than by slow accumulation of small differences" (Goldschmidt, 1955).

It is clear that such a hypothesis should bring about a rebuttal from the neo-darwinians who of course believe that speciation occurs by the slow accumulation of small differences.

Dobzhansky (1951) pointed out that, "in sexual and cross-fertilizing species, a great difficulty is encountered in the establishment of any reproductive isolating mechanism in a single mutational step. Since mutants appear in populations at first as heterozygotes, inviable and sterile heterozygotes are eliminated, regardless of how well adapted might be the corresponding homozygotes. This consideration is fatal to Goldschmidt's theory of evolution by systemic mutations". However, in recent studies on speciation in frogs and mammals, it was pointed out that evolution at the level of proteins was very similar in both groups. Since the rates of speciation were vastly different, it is clear that point mutations are an inadequate explanation of speciation. Hence, "the rapid rate of gene arrangement in mammals parallels both their rapid anatomical evolution and their rapid evolutionary loss of the potential for interspecific hybridization. Thus, gene arrangements may be more important than point mutations as sources for evolutionary changes in anatomy and way of life" (Wilson, Sarich and Maxson, 1974). It is becoming clear that one is going to have to wrestle with the difficulties of Goldschmidt's systemic mutations.

If the repatterning of the chromosomes could spread in a population by means other than sexual recombination, then Dobzhansky's objections could be met. That viruses may spread in a population by infection is obvious. More recently the interactions between viruses and chromosomes have received attention because they may cause somatic mutations leading to cancer and aging. Some of these interactions lead to, "three types of change: single chromosome breaks, chromosome pulverizations and cell fusion with spindle abnormalities" (Nichols, 1969). If one could combine viral infection with gross chromosomal changes in the germ line, one would then have speciation by infection.

The specificity of the interaction between virus and chromosome must be considered. B. McClintock has studied genes in maize which altered the mutability of adjacent genes. An unusual feature is that these genes change their location either on the same chromosome or on other chromosomes. This ability to hop from location to location was compared to various lysogenic systems in bacteria (e.g. λ viruses) (Jacob, 1959).

The integration of λ with the E. coli chromosome requires enzymes coded for by the viral genes. These enzymes lead to a very specific integration of the viral genes into the bacterial chromosome. The similarities between lysogeny and tumor viruses (e.g. SV40 and polyoma) are numerous. The integration of these viruses occur at specific locations on the chromosome. Thus evidence is accumulating that the virus-chromosome interactions are specific (Stanier, Doudoroff and Adelberg, 1970).

The virus has been instrumental in our dissection of the naked gene. The virus may play an important role in our attempts to analyze cell evolution, differentiation and speciation. L'Heritier (1970) summed it up as follows, "during the last years viruses have been favorite materials for research in

molecular biology. For a longer time they have chiefly interested pathologists. Perhaps the time has come to look at them not merely as inducers of biochemical and pathological processes, but as part of the ever-evolving living world".

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