Are viruses our oldest ancestors?

Karin Moelling

Humans have a skewed view of viruses because we only notice them if they cause disease. In reality, however, viruses are much more than pathogens. HIV and influenza cause frightening health threats, but 10^{19} HIV particles worldwide are basically nothing compared to 10^{33} total number of viruses on our planet. Viruses are present in every species and every ecological niche, and affect every organism. They even influence the global climate by regulating the population densities of microorganisms—and thereby nutrient availability—in the oceans [1]. We are the invaders of the viral world, not vice versa.

Not surprisingly, viruses have been a major factor in evolution. They might have preceded and enabled the emergence of cells and thus provide us with a glimpse into our evolutionary past. Chemical reactions in the primordial soup created increasingly complex RNA molecules. This eventually gave rise to ribozymes, catalytically active molecules that have been demonstrated to replicate and evolve in a test tube [2]. Ribozymes are still with us today as viroids in plants: hairpin loop-structured catalytic RNAs that do not code for proteins and lack a protein coat. Some plant viruses contain stabilizing structures, such as tRNAs, which can fold back to the RNA and bind to amino acids—could this have marked the beginning of peptide synthesis? Moreover, most RNA viruses have ribonucleoproteins that increase the catalytic activity of ribozymes and stimulate replication [3], which might have further accelerated evolution. The variability and flexibility of RNA viruses was essential to the early stages of life.

The reverse transcriptase and its close relative telomerase paved the way to DNA: they still generate DNA from RNA in retroviruses, embryos and cancer cells [4]. The term reverse transcriptase is, in fact, a misnomer: if RNA preceded DNA, then reverse transcriptase was the first 'real transcriptase'. DNA genomes might have evolved from pararetroviruses such as hepatitis B (HBV; [4]), which do not integrate but allowed integration of retroviral DNA or other viruses so as to grow a DNA genome. Given their incomplete viral double-stranded DNA and their pregenomic RNA, HBV might have established the central dogma and formed the precursor of the nucleus—thus, retroviruses might have helped to build the first cells.

Findings also challenge the paradigm that viruses are only parasites that depend on their hosts to proliferate. The discovery of giant viruses, which were first misinterpreted as bacteria, provides new insights into how cells could have evolved. The size of these viruses, the presence of ribosomes and infectious virophages and other properties suggest that they might be an ancient link between viruses and bacteria [5]. They might have been arrested during evolution on their way to bacteria or regressed from bacteria and stayed around as a dead-end branch in the tree of life.

Viruses have also been a major factor for the evolution of all life. They helped to build the genomes of their host species, including humans. Almost 50% of our genome is comprised of retroelements. If the shortest retroelements, 500,000 long terminal repeat promoters, were once full-length retroviruses, they would add up to the size of our genome. Are we therefore the descendants of viruses? This is impossible to prove, because viral footprints disappeared with time.

The ability of retroviruses to integrate into host genomes influences gene regulation and enables the transfer of genes, such as oncogenes, or regulatory elements within and across species. This so-called horizontal gene transfer has been the main driver of evolution from bacteria to humans. Is it still a major factor in human evolution today? Billions of replicating HIV could have been a large-scale experiment for gene transfer; however, surprisingly no new oncogenes arose.

Bacteriophages are the most successful entities on our planet as judged by their abundance, their efficiency in replication and gene transfer and their ability to adapt. Almost all phages have replaced RNA with double-stranded DNA genomes; they are the front-runners in evolution, whereas RNA plant viruses seem to be the laggards—this could be explained with the vastly different replication rates of their hosts. It might also explain why cut-and-paste DNA transposition is active only in plants; in mammalian genomes, it terminated about 35 million years ago and jumping retroelements increased genome size and diversity.

The evolution and abundance of phages could also provide clues for the future of humans. It is easy to envisage a scenario of overpopulation and lack of food. If this happens in bacterial populations, phages kill their starving hosts and thereby recycle nutrients for the surviving cells. By analogy, human viruses such as HIV or influenza already influence human population dynamics. In addition, we do not know what other viruses lurk in our environment that could cause a major pandemic if overpopulation and malnutrition exert their toll on the human population. Bacteria and phages undergo cyclic phases of overpopulation and mass death. Those cells that survive the viral onslaught can regrow in another environment and evolve with new properties. Major pandemics that cause mass death might therefore allow us to survive in a changed world. Thus, viruses might not only be the doom but at the same time the hope of humanity.

CONFLICT OF INTEREST

The author declares that she has no conflict of interest.

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