Advanced Studies in Biology, Vol. 5, 2013, no. 9, 423 - 430
HIKARI Ltd, www.m-hikari.com
http://dx.doi.org/10.12988/asb.2013.3835

Origin of the Viruses and

Their Evolutionary History

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Abstract. The human immunodeficiency virus (HIV) originated via a process of natural evolution, probably emerging from the primate SIV reservoir into the human population via hunting or other behavior involving contact with the blood of these animals. A particular subspecies of chimpanzee, the Pantroglodytes troglodytes, has been recognized as the most probable original source of human infection. Analysis of viral genetic sequences has allowed researchers to estimate that the native strain of HIV originated in 1931. In the West, sexual behavior patterns and injecting drug use subsequently began the epidemic.

Polymerase Chain reaction (PCR), is a technique in molecular biology that amplifies a specific region of deoxyribonucleic acid (DNA), and has been useful in the molecular characterization of viruses.

The Variola major, the virus that causes the smallpox, lethal virus in the 30% of the cases, was eradicated in 1979 in the human species, thanks to a capillary vaccination on global scale. It has now become a “historical footprint” in two known laboratories, one in the USA and another in Russia, leaving no obvious source for its often-theorized use as a bioterrorist weapon. Nevertheless, mass vaccination against smallpox continues to be a leading initiative in Western countries to guard against bioterrorist attack.

Keywords: HIV, Herpesvirus, HPV, Smallpox

Origin of the HIV

The evolution of the AIDS virus and its migratory phenomena can be considered as a good example of how several viruses originated. Although various hypotheses have been proposed during the last 25 years, it is now clear that the human immunodeficiency virus (HIV) was formed through a process of natural evolution. The theory on the origin of the HIV that has found the greatest consensus maintains that this virus is derived from the mutations of a virus that infects some species of African chimpanzee, the Simian immunodeficiency Virus (SIV). Through molecular biology studies, it has been possible to establish a relationship between the HIV and the SIV, identifying a 98% genetic homology between these two viruses, and building a solid viral genealogical tree. The infection from HIV would be therefore a zoonosis, that is, an infection transmitted to the man by other animal species: HIV probably migrated from the primate reservoir to humans by hunting or by tribal rites that implied contact with the blood of these animals. SIV would then have become HIV via various genetic mutations over many years. This hypothesis has been confirmed by the study of a group of researchers of the University of Alabama in Birmingham, presented at the Sixth Conference on Retroviruses and Opportunistic Infections held in Chicago in February 1999, where a particular kind of chimpanzee, Pantroglodytes troglodytes, has been recognized as the most probable source of infection in humans.

HIV would therefore have probably existed for long time in the small tribal communities of Africa. Urbanization, especially during the colonial period, caused mass migrations and the spread of more liberal customs, with a consequent increase of sexual contact between individuals from different areas (as well as prostitution). These movements and trends may have favored the local spread of HIV, creating a "cluster" of infected individuals, on which the future expansion of the infection was based. Subsequently, various factors such as the contact with the West, the use of unsterilized hypodermic syringes in vaccination campaigns, and the use of blood transfusions in cases of malaria, favored the wider spread of HIV, and its transmission to the West. From there, sexual liberation and drug addiction exacerbated this into the epidemic that became apparent in the '80s and '90s. An article published in the journal Nature from a group led by David Ho (director of the Aaron Diamond AIDS Research Center in New York), announced the discovery of traces of the genome of HIV in a blood sample belonging to a man who lived in Kinshasa (Congo) and died in 1959. By molecular analysis of this virus, compared

with more recently isolated viral strains, it has been possible to estimate the origin of the HIV as being before 1940, thereby suggesting the hypothesis that the transmission of the virus from chimpanzee to man first occurred approximately 70 years ago. In a follow-up paper, published in the journal Science, further analysis of the genetic sequence of the virus, aided by sophisticated statistical models, has allowed researchers to estimate that the native strain of HIV originated after 1931.

Evolutionary history of the viruses

When studying such a major component of the biosphere as the viruses, it is important to apply a molecular approach that allows their isolation and the determination of individuality among the various strains, types and subtypes of the same family. PCR, is a key technique for this, and its utilization with new and existing diagnostic methods for environmental and medical surveillance is a powerful approach to national health security. It creates an opportunity to: detect unusual microbiological events in the environment; assess the medical and public health significance of these events; position the public health and emergency response teams to respond quickly and appropriately to biothreats; and provide real-time health benefits to the population while maximizing early detection and appropriate responses to potential bioterrorist acts.

Interaction between viruses and host

Having entered the host cell, viruses can give rise to acute, latent or persistent infection. In the former case , the virus enters the body, replicates over a limited period of time and is then completely eliminated by the host (or causes its death). The latter types of infection are characterized by alternating replication of the virus and its latent infection, or the onset of chronic and continuous replication.

The site of latency is different for each subfamily of herpes viruses, but these are usually located in areas of the body where they are protected from the immune system [9].

There are molecular mechanisms that allow the viral genome to remain in a latent state [11], and those leading to exit from latency and resumption of the lytic cycle of viral replication [6].

HSV1 and 2 infect epithelial cells and yield latent infections in the neurons [14]. HSV 1 is classically associated with oropharyngeal lesions, while HSV 2 primarily infects the genital mucosa.

The Varicella Zoster Virus (VZV) causes the disease known as chickenpox in primary rash and establishes a latent infection in neurons, which [2], if reactivated,

causes herpes zoster (shingles).
The *Polyomaviridae* family includes, among others, JC Virus (JCV), BK Virus (BKV) and SV40. The primary infection caused by these viruses is asymptomatic and occurs during childhood, followed by latency [7];[10].
Reactivation of Polyomavirus depends on the function of the host immune system: when it is no longer competent or undergoes immunosuppression, the virus reactivates its replication and causes disease.
Hepatitis viruses B and C are associated with hepatocellular carcinoma. Altogether, over the 50% of all liver cancer worldwide are attributable to hepatitis B infection, for which an effective preventative vaccine is available.
Human Papilloma Viruses (HPV) have been correlated with cervical cancer, with genotypes 16 and 18 being considered particularly carcinogenic in humans [15]. In 2006 the FDA released the first vaccine against HPV.
The viral proteins E6 and E7 are able to inhibit oncosuppressors during the process of malignant transformation [1];[13].
HCV belongs to the Flaviviridae family. Its infection can remain stable and cause mild hepatitis, liver cirrhosis or it may evolve in hepatocellular carcinoma [4].
The main strategy to evade the immune response is the genetic variation faced by the viral genome.
The consequence of the heterogeneity of HCV gene expression and its ability for genetic and then phenotypic mutation, are therefore at the base of such a high rate of chronic infections, of the not efficacy of the therapies and also of the difficulty of preparing vaccines.

Smallpox virus and vaccination

From the " Malignancy" of the oncogenic viruses now we move to that one of the Smallpox virus and the possibility for such viruses to be used as weapons in bioterrorism even if they were eradicated by a global vaccination, real pacemaker of other Viral Vaccines.
As it is now known, the "Variola major" virus that causes smallpox, which was lethal in 30% of cases, was eradicated, thanks to a capillary vaccination on a global scale in 1979 . It has now become a "historical footprint", guarded under maximum security and the superintendence of the World Health Organization, in two known laboratories, one in the USA and another in Russia. Since there are, in theory, no more strains of human smallpox elsewhere on the planet, a major question is where the new strains required to buil a bioterrorist weapon could possibly come from. Despite this, the debate on the vaccinations in recent times is closely bound to the

threat of a bioterrorist attack; these arguments define lurid, apocalyptic scenerios that have received disproportionate coverage in the mass media, and have already resulted in a whole series of "exercises", such as those held in England in December 2002, to face a hypothetical attack with smallpox virus.

Meanwhile, it must be said that, despite innumerable articles, novels and films based on the scenario, an isolated bioterroristic attack would not seem to have a very large chance of instigating a devastating epidemic. Unlike biological attack conducted by an army (prepared for by using conventional bombardments to destroy command infrastructure, sanitary systems and buildings, and causing refugee crowding before launching an attack with pathogenic germs or toxins), bioterrorism would presumably launch an attack on a focused target, with an entire region able to react to the threat. This hypothesis is supported by declassified reports, such as the epidemiological studies on people successfully hospitalized following the experimental dissemination of a non-harmful bacterial agent by the US Department to the Defense in the New York subway in 1956. A less deliberate example occurred in England in 1962 when a researcher, George Bacon, became infected with a modified strain of Yersinia pestis (bubonic plague) at the biological warfare facility of Porton Down, UK, and exposed the outside world to this infection before dying. Continuing on this theme, another example is the accidental release of smallpox from the University of Birmingham, UK in 1978, which killed three people. Why did two dangerous microorganisms, Yersinia pestis (made more lethal by modification at Porton Down) and Variola major, both transmissible through the respiratory route not produce a catastrophic epidemic? Numerous studies have been compiled to address the incidents, and all have described the initial sanitary measures as being insufficient. Regarding the Birmingham incident, the role played by antivariola vaccination, obligatory for all in Europe at that point but poorly practiced in England, was also pointed out. But then, why was there no catastrophe? The ‘why’ to seem would be, (aside from the still-unclear mechanisms governing epidemic dynamics), the existence of a solid health infrastructure did not collapse at the announcement of the infection. In this sense, perhaps the element that could transform a bioterrorist attack in a catastrophe is in fact the irresponsible emphasis the mass media devote to this threat at present, which might be able to instigate a panic, with a consequent mass exodus from the area, spreading the epidemic.

The use of mass-vaccination to protect against a terrorist attack using the smallpox virus has clearly been discarded, as indicated by a document published in the New York Times, "Supplemental Recommendation of the ACIP on Use of Smallpox" compiled June 20 2002 by the Advisory Committee on the practices of immunization and submitted to the Department of Human Health of the United States (HHS) and to the Center for the Control of the Epidemics (CDC), which approved in Despite this

the proposal of a vaccination of mass against the smallpox (of 500.000 people in the United States only) continues to be in the front among the "initiatives" of the Western countries to face a bioterroristic attack of which (beyond the case of the "letters at the anthrax" that allowes to glimpse responsibility not surely referable to some fanatical person) no comparison is found.
Although the threat of these infectious diseases, and therefore the problem of administering vaccinations, seem to be relatively unimportant issues in Western countries, in many areas of the 'Third World' extremely poor sanitary conditions and the unattainably high cost of vaccines could result in a death sentence for millions of people.

Evolution of man and genomic mutation. Future perspectives

During the eight-million-year evolution from the state of monkey to man, the accumulation of genomic mutations amounted to only 2%; some viruses, however, can accumulate a similar proportion of genomic mutations during just 5 days of replicative activity.
Type A influenza viruses have a strong tendency to mutate, changing their own structure rapidly, and this genetic variability can be divided into antigenic drift, with minor changes that are associated with sporadic cases or small outbreaks, and antigenic shift, with more significant changes and the creation of new subtypes, which is responsible for large epidemics and pandemics [3];[5];[8].
Methodologies for extracting virus and non viral antigens, and cancer vaccine development techniques allow further steps in understanding the role of viruses and the strategies of the immune system to produce humoral and cellular antibodies.
Peptide search in the tumor liberated protein and cancer proteomics represent the most advanced discovery in anticancer peptide vaccines [12].

The author declares no conflict of interests.

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Received: August 15, 2013