The Biological Nature of AIDS Virus

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Acquired immune deficiency syndrome (AIDS) is a viral disease that destroys the immune system of the human body. Consequently, persons with AIDS are highly susceptible to infectious diseases. They are also at an increased risk for the development of some forms of cancer, since the immune system not only protects the body from infectious microorganisms, but also recognizes and destroys abnormal cells such as cancer cells when they arise in the body.

Many of those diagnosed as having AIDS are homosexual males. The syndrome has also been diagnosed among drug addicts using intravenously administered drugs, hemophiliacs treated with medication derived from donated blood and people who have received blood transfusions. Furthermore, the virus can be transmitted by heterosexual activities, and from an infected woman to her unborn child or during birth of the child.

It is not my intention to discuss herein the social implications of AIDS. Such matters are receiving considerable attention in the popular press. However, because of widespread concern about AIDS, including controversy over the presence in the classroom of students infected with AIDS virus, it is likely that biology teachers would be interested in the biological nature of the etiological agent of AIDS.

The Virus

The virus that causes AIDS is known by three names: human T-cell lymphotropic virus type III, lymphadenopathy associated virus and AIDS-associated retrovirus. The differences reflect the naming of the virus after its isolation by different investigators. At present, there is no agreement on what is the most appropriate name for the virus. There is a movement away from naming viruses after diseases, as many viruses cause more than one disease. For example, chickenpox virus is now known also to cause shingles. For convenience, I will refer to the causative agent of AIDS as AIDS virus herein.

Whether viruses are living things or not is still a debatable point. However, viruses do have the two most important characteristics of living things. One, they have genetic material and give rise to progeny with like characteristics. Two, because they have genetic material they can undergo genetic change (i.e., like living things) by mutation and recombination.

Viruses contain either DNA or RNA, but never both kinds of nucleic acid. The genetic material of some viruses is DNA (e.g., herpes virus), while the genetic material of other viruses is RNA (e.g., influenza virus). Whether DNA- or RNA-containing viruses, during virus replication the genetic material is duplicated using one strand of the nucleic acid as a template for the formation of another strand.

AIDS virus belongs to a large and well-studied family of viruses, the Retroviridae. Retroviruses are spherical in shape. Their genetic material is single-stranded RNA. The RNA is surrounded and protected by a protein capsid, or coat, and this in turn is surrounded by an envelope consisting of lipid and protein and carbohydrate (Fraenkel-Conrat & Kimball 1982). For a virus to infect a cell there must be an affinity between the virus and the cell. Since the envelope is the outer limit of retroviruses, it is the envelope that determines what cells the viruses can infect.

Retroviruses are so named because, by means of an enzyme called reverse transcriptase, they use RNA as a template for the synthesis of DNA. This is a reversal of the usual process of transcription of DNA into RNA. The action of reverse transcriptase makes it possible for genetic material from a retrovirus to become incorporated into the chromosomes of an infected cell (Fraenkel-Conrat & Kimball 1982). Retroviruses possess the genetic information necessary for the synthesis of reverse transcriptase, and this unusual enzyme has never been found anywhere else in nature except in retrovirus-infected cells and incorporated into retroviruses.

Infection With The Virus

When AIDS virus infects a cell, its envelope and capsid are removed. The single-stranded viral RNA is used as a template for the formation of an RNA-DNA hybrid molecule. To do this requires reverse transcriptase, an RNA-directed DNA polymerase. The DNA of the RNA-DNA hybrid serves as a template for the formation of a strand of DNA, which in turn is used as a template for the formation of a complementary strand of DNA. This gives rise to a double-stranded DNA molecule, which is then integrated into host cell DNA. Production of progeny viruses is transcribed from the integrated viral DNA. During replication of viruses, viral components are produced in great abundance using biosynthetic mechanisms of the host cell. Progeny viruses are then synthesized from the components. One virus gives rise to numerous progeny.

Most retroviruses cause either malignant solid tumors or leukemias in animals. Retrovirus-induced cancers are known in reptiles and birds as well as a broad-spectrum of mammals (Fraenkel-Conrat & Kimball 1982). Human T-cell leukemia/lymphoma is caused by a retrovirus; the first unequivocal proof of a virus causing cancer in human beings. AIDS virus is one of the few retroviruses that does not cause cancer. Indeed, it destroys cells, and thus has the opposite effect to the uncontrolled cell proliferation of cancer. It should be pointed out that cancer in patients with AIDS is due to the immune deficient state. Cancer-causing viruses either carry into cells the genes responsible for cancer, or infection of cells with a virus results in the expression of genes present in the cell prior to virus infection.

Two types of lymphocytes have a role in the immune responses of mammals, B-lymphocytes (B-cells) and T-lymphocytes (T-cells). B-cells multiply and differentiate into plasma cells that produce antibody. T-cells have a variety of functions in immune responses, and several sub-sets of T-cells are known. A sub-set called T-helper cells stimulate the multiplication and differentiation of B-cells into plasma cells, and so are involved in the production of antibody. Little or no antibody is produced without the help of T-helper cells. AIDS virus infects and brings about the destruction of T-helper cells. The severity of the immune deficiency depends upon the rate of destruction of T-helper cells and the rate of their replacement (Seale 1985).

In cases of infection with AIDS virus, antibodies appear to have little or no capacity to neutralize the virus. The reason for this is not known, but possibly the antibodies react with sites on the surface of the virus that are not involved in the attachment of the virus to its host cell. Attachment to the host cell membrane is necessary before a virus can enter an animal cell.

Antigens are proteins, and sometimes polysaccharides, that induce animals to make antibodies against them. Different isolates of AIDS virus show variation in the gene that codes for an envelope glycoprotein, the major antigen for stimulating the production of antibody to the virus (Seale 1985). Antigenic variation will make it difficult to produce a vaccine against AIDS. The reason human beings have influenza time-and-time again is because influenza virus frequently undergoes antigenic variation. Therefore, antibodies present as a result of previous infection cannot protect the body against infection by a variant of influenza virus. Because of antigenic variation, vaccines against influenza virus are not too effective. Antigenic variation is not the reason for all viral diseases we get more than once. Having the common cold over and over again is due to the large number of different viruses that can cause the disease.

Cases of progressive encephalopathy caused by AIDS virus have been reported (Seale 1985). Although AIDS virus is responsible for this brian disease, persons with the disease do not have immune deficiency. Thus, AIDS virus can cause a disease other than AIDS.

Visna virus causes a slowly progressive brain disease in sheep. This virus, like AIDS virus, is one of the few retroviruses that does not cause cancer. Visna virus was discovered about 30 years ago. Investigations have shown that the virus has a 100 percent mortality rate within about two-thirds of the normal life span of sheep. Visna virus-infected sheep do not have immune deficiency.

As noted above, it will be a difficult task to develop a vaccine to prevent infection with AIDS virus. What about agents for treating AIDS virus infection? Again, the answer is not very cheerful. Bacterial diseases have become largely curable through the use of antibiotics. However, these methods are not applicable to virus diseases. The antibiotics that are used against bacterial infections attack critical, and quite often unique, processes of bacteria. Viruses utilize host cell metabolism, and agents that prevent virus replication interfere with normal cellular activities (Fraenkel-Conrat & Kimball 1982). Regarding retroviruses, another problem with respect to antiviral treatment is the fact that virus infection is well established, and viral DNA is integrated into host cell DNA, before the person shows early symptoms of disease. An agent that prevented expression of integrated viral DNA would have to be taken continuously, since the integrated viral DNA acts as if it were part of the normal genome of the host cell. Lymphocytes have the ability to multiply, and an antiviral agent that could selectively destroy AIDS virus-infected T-cells would allow normal T-cells to multiply and replace destroyed cells. Such an ap-

proach would not be possible with AIDS virus-infected neurons, since after birth of an individual their neurons do not multiply, and consequently destroyed neurons are not replaced.

AIDS is a new disease, and naturally there is interest in where the etiological agent of the disease came from. Information on the origin of AIDS virus is sketchy at the moment. Possibly the virus originated in central Africa, and has crossed the species barrier from monkeys to human beings (Newmark 1985). Contributing to this possibility is the fact that a significant number of healthy African green monkeys that have been investigated had antibodies in their blood that react with AIDS virus. Viruses generally infect only one or a few species. The reason for this is the inability of a virus to infect cells of different species owing to a lack of affinity between the virus and the cells. Even if, as on some occasions, infection of cells takes place, the virus cannot replicate, since it is in a cell that cannot provide the necessary precursors and metabolism for virus replication. Natural crossing of species barriers by viruses is not easy to ascertain, but in recent years some viruses have been observed to do so. Lassa virus, the causative agent of Lassa fever, crossed from rats to human beings. Marburg virus, the etiological agent of Marburg disease, crossed from monkeys to human beings. Both Lassa fever and Marburg disease have a high mortality rate in human beings, but fortunately the causative viruses are not easily transmitted to or among the human population at large.

Infection with AIDS virus occurs mostly in people with certain lifestyles, and there is no evidence that the virus will become widespread among all lifestyles. With the exception of infants born to infected mothers or sexual partners of infected persons, not one family member of more than 13,000 persons with AIDS reported to the Centers for Disease Control have become infected with the virus, despite what in many cases was years of close contact with an infected person, including hugging, kissing and sharing of tableware and bathrooms (Centers for Disease Control 1985). It is now more than four years since the first cases of AIDS became known, and although development of the disease is slow, if the virus was easily transmitted, some cases of AIDS would have been seen by now among the many thousands of family members living with the 13,000 reported cases of the disease. In addition, there have been no cases of physicians and nurses and other healthcare workers involved in the treatment and care of AIDS patients contracting AIDS.

References

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