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MORPHOLOGY OF THE RETROVIRUSES ASSOCIATED WITH AIDS AND SAIDS

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Thin section electron microscopy of tissue culture preparations of viruses associated with AIDS and SAIDS have shown that the mature particles have a similar morphology following budding from the cell membrane. The model provided explains the various core morphologies seen in section and provides a basis for identifying these agents in clinical tissues.

Introduction. In the past year several reports have appeared which describe the detection of retroviruses associated with the lymphadenopathy associated syndrome (LAS) (1-5) and the isolation of retroviruses from patients with the acquired immunodeficiency syndrome (AIDS) (6-10). In addition, retroviruses were isolated from monkeys with the simian acquired immunodeficiency syndrome (SAIDS) (11-17). With both the human and monkey diseases, some of the electron micrographs show that the viruses possess bar-shaped cores whereas in other photographs the cores appear as triangular shapes, a central or eccentric electron dense dot, or the cores may be absent (2-5,7-8,15). A bar-shaped core and a reverse transcriptase (RT) with a preference for Mg^{++} for maximum activity are characteristics shown by some members of the D type group of retroviruses of which Mason-Pfizer monkey virus (MPMV) is the prototype (18-19). We have recently examined tissue culture preparations of the HTLV-III virus which was isolated from an AIDS patient and the IDB-1 virus from a SAIDS monkey by thin section electron microscopy. We find that both viruses are assembled on cell membranes and they possess cylindrical cores which can appear in various forms depending on the plane of section. This information should be useful for the classification of these agents and for identifying the viruses in clinical tissues.

Materials and Methods. Immortalized T-lymphocytes producing high levels of HTLV-III virus were kindly supplied to us by Dr. Robert C. Gallo, NCI, Bethesda, MD and rhesus monkey bone marrow cultures containing the IDB-1 SAIDS virus isolated in our laboratory, were used in our study (6,14). Cell suspensions were centrifuged at low speed, the pellets were resuspended in 5% glutaraldehyde in phosphate buffered saline (PBS) and allowed to stand for one hr at 4°C. These suspensions were again pelleted at low speed, washed twice in PBS and post fixed in 1% OsO_4 in cacodylate buffer for one hr. The cells were pelleted, dehydrated in ethanol dilutions, cleared in propylene oxide, embedded in Arablite 502 and cured overnight at 70°C. Thin sections were double stained with uranyl acetate and lead citrate and examined in a JEM 100 CX II electron microscope at an instrumental magnification of 36,000.

Results. Figures 1 and 2 are photomicrographs of cells infected with HTLV-III (AIDS) virus and the IDB-1 (SAIDS) virus respectively. Both preparations show free virus particles but no viral core particles are evident in the cytoplasmic matrix as is typical for MPMV, the prototype D retrovirus. AIDS and SAIDS viruses have similar morphology. There is variation in the appearance of the cores which relate to the plane of section. The electron dense cores appear to be cylindrical. Figure 3 shows

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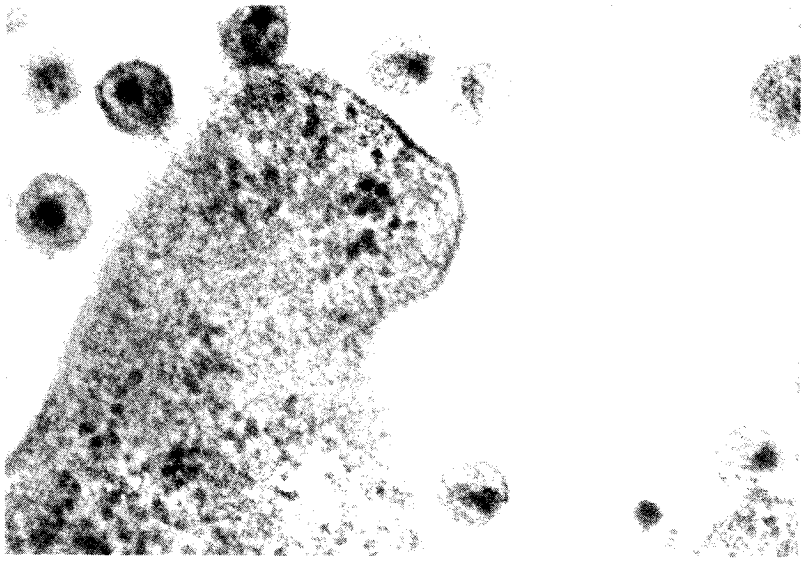

Fig. 1. HTLV-III AIDS virus Mag. 100,000 X.

diagrammatically the appearance of the particle from budding through core development (arrowed sequence) and the principal forms of cores encountered (A, B, C, D, E) when the virus particles are cut in various planes (A^1, B^1, C^1, D^1, E^1). Consequently, the core may be absent (A and A^1), triangular (B and B^1), dense and central (C and C^1) or eccentric (E and E^1). D and D^1 represent cross sections perpendicular to the cylindrical core which is often seen to be hollow in the virus preparations. The core may also appear as a complete cylinder as shown in the central diagram. There is evidence of a fine fringe on the surface of the virus. Aberrant forms of both viruses probably occur as well.

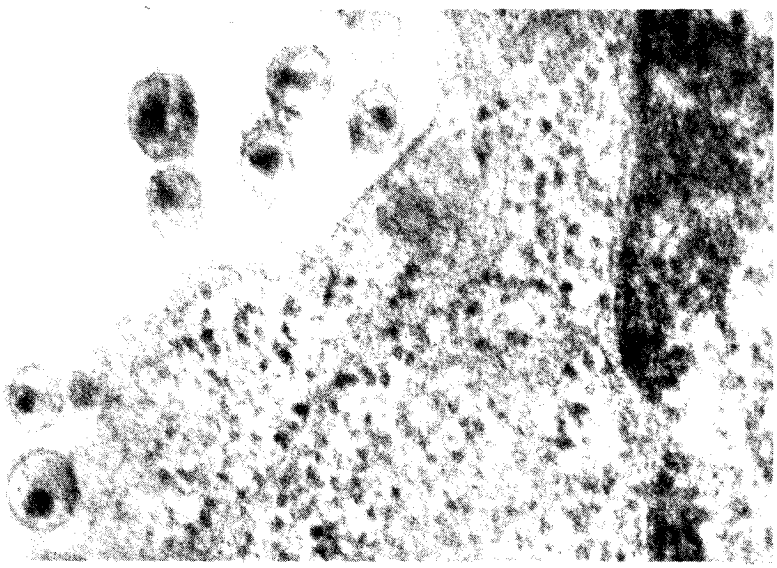

Fig. 2. IDB-1 SAIDS virus Mag. 100,000 X.

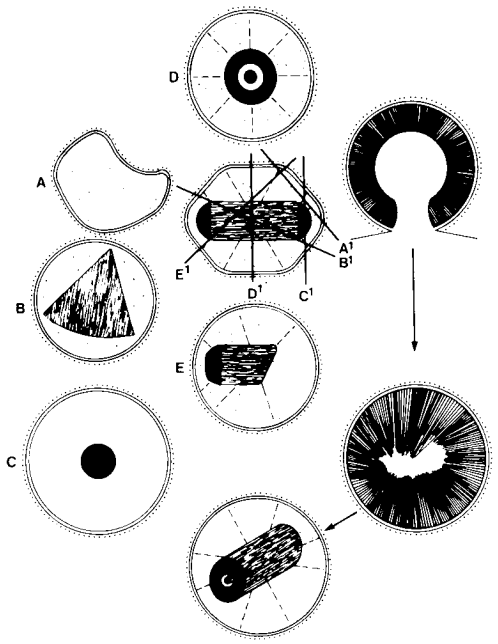

Fig. 3. Diagrammatic representation of the development and appearance of AIDS and SAIDS associated viruses when the virus particles are cut in various planes.

Discussion. We consider that the absence of intracytoplasmic core particles in the cytoplasm of the cells in our preparations and those of published micrographs (6,7,8,15) is a characteristic which distinguishes HTLV-III (AIDS) and IDB-1 (SAIDS) from the D type retroviruses. A common characteristic shared by HTLV-III, IDB-1 and MPMV is a cylindrical core. The budding mechanism is similar to that seen with C type retroviruses. In addition, the cylindrical core appears to condense in the particle subsequent to budding, analogous to the core condensation in C type retroviruses. From published electron micrographs (1-5), it would appear that the lymphadenopathy associated virus (LAV) and immunodeficiency associated virus (IDAV) isolated from AIDS patients in France have a morphology similar to that described here. Consequently, on morphological grounds, HTLV-III, LAV, IDAV and the SAIDS virus appear to have developmental characteristics of both C and D type retroviruses. While the preference for Mg^{++} for RT activity is a D type characteristic, it is also a B type characteristic and may apply to other retroviruses as well. Although some intracytoplasmic core particles have been described for the SAIDS virus (17), they were not as numerous as those shown in MPMV preparations (18) containing intracytoplasmic A particles and may not be the major source of budding virus particles in SAIDS infected cells. On this basis, the SAIDS agent would be closer to MPMV than would the AIDS agents. AIDS and SAIDS viruses, and possibly other retroviruses (20), appear to have characteristics of both type C and type D groups and may constitute a distinctive morphological group of retroviruses. The cylindrical core characteristics of the AIDS and SAIDS viruses should be of value in identifying these agents by electron microscopy in cultures and in clinical tissues.

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