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RESEARCH NOTE

ENDOCYTOSIS OF THE HUMAN IMMUNODEFICIENCY VIRUS *IN VITRO*

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Enveloped RNA viruses are known to enter cells by two different ways (Choppin & Scheid, 1980, *Rev. Inf. Dis., 2* :40-61; Mellman et al., 1986, *Ann. Rev. Biochem, 55* :663-700). The virus membrane fuses with the cell surface membrane (e.g. Sendai virus) or the virus is taken up by coated pits and coated vesicles into acidified endosomes, where the fusion of viral and vacuolar membrane occurs (e.g. Semliki Forest virus). Both processes lead to the liberation of the viral RNA into the cytoplasm of the host cell.

In the case of the AIDS related human immunodeficiency virus (HIV), many diagrams in the literature, including the cover picture of the abstract volume of the III International Congress on AIDS (Washington, USA, June 1-5, 1987), propose a direct fusion of the HIV membrane with the T4 lymphocyte surface membrane. This model is mainly based on the observation that the interaction of the envelope glycoprotein of HIV with the CD4 cell surface receptor induces cell-cell fusions and syncytia formation in the lymphocyte culture. A similar interaction was thought to lead to the fusion of virus and cell surface membrane (Lifson et al., 1986, *Nature, 323* :725-728; Haseltine & Sodroski, 1987, *Ann. Inst. Pasteur/Virol., 138* :83-92). Furthermore the action of lysosomotropic weak bases and proton ionophore,which are known to prevent the uncoating of viruses in acidic endosomes and secondary lysosomes, did not inhibit the infection of culture cells by HIV (Stein et al., MP.12; McClure et al., MP.20, 1987, III Int. Congr. AIDS, Washington). Recently Stein and colleagues (1987, *Cell, 49* :659-668) could observe by electron microscopy in some occasions the fusion of HIV with VB cells 2 min after infection at neutral pH and 4ºC. These authors did not find virus endocytosis in their culture system.

Studying the ultrastructure of a H9 cell line chronically infected with the HTLV-III isolate of HIV (a system generously supplied to our institute by Dr. R. Gallo, USA), we could never observe signs of fusion of the virus membrane with the cell surface. On the other hand some cells presented virus particles near or inside coated pits and in coated vesicles (Figs. 1-4 and Bauer et al., 1987, An. XI Colóquio Soc. Bras. Mic. Elet., Caxambu, Brasil, September 1-3, p. 45-46). Dr. Luc Montagnier also showed photographs of the endocytosis of HIV by coated pits at the I Pan-American Teleconference on AIDS (Quito, Ecuador, September 14-15, 1987). On one occasion we could find a virus particle inside a vacuole near a Golgi zone and one inside a multivesicular body (Figs. 5, 6). These results suggest that an endocytosis up to multivesicular endosomes (Wileman et al., 1985, *Biochem. J., 232* :1-14) may occur in the case of HIV infection, comparable to the situation of Semliki Forest virus (Marsh et al., 1983, *Cell, 32* :931-940) and fowl plague virus (Matlin et al., 1981, *J. Cell Biol., 91* :601-613). Endocytosis by coated pits and vesicles into endosome-like vacuoles of culture cells could also be found with retroviruses like the avian leukosis and sarcoma viruses (Dales & Hanafusa, 1972, *Virology, 50* :440-458). It is possible, regarding the mentioned observations, that, depending on culture conditions, both fusion with cell surface membrane or endocytosis and posterior fusion with vacuolar membrane probably in a pH-independent way (Stein et al., cit op.) occur in HIV infections.

Further studies are necessary for the exact understanding of the virus entry into the cell, which also constitutes an important target for antiviral substances in the acquired immunodeficiency syndrome.

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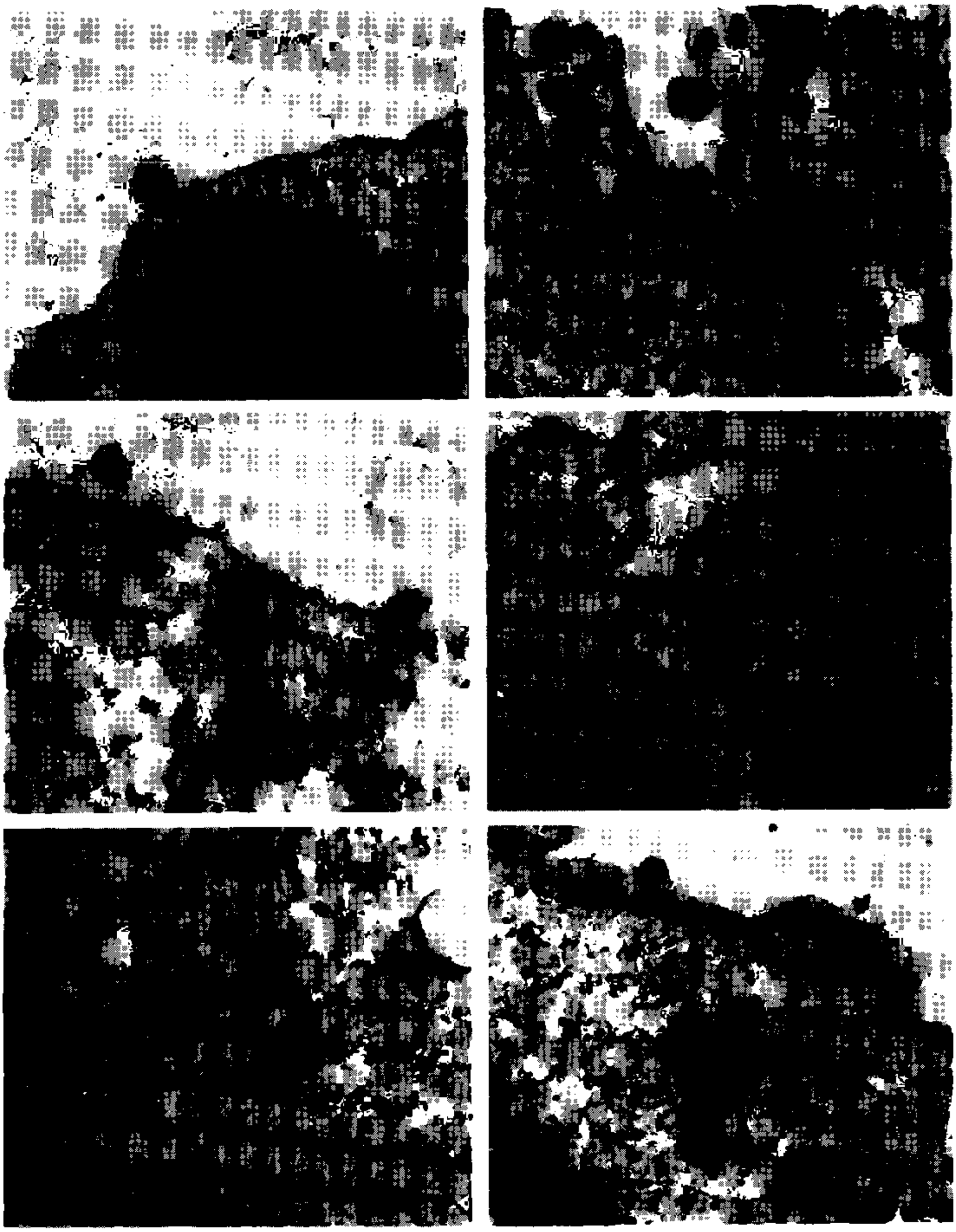

Endocytosis of the human immunodeficiency virus in a chronically infected H9 cell culture. Fig. 1: Virus particle adsorbed to the H9 cell surface, lying at the border of a coated pit (49000x). Fig. 2: Virus inside a coated pit (47900x). Fig. 3: Virus particle in a deep invaginated coated pit (54000x). Fig. 4: Virus inside a forming coated vesicle (55500x). Fig. 5: Virus particle in a vacuole near a Golgi zone (54100x). Fig. 6: Virus inside a multivesicular body (54100x).