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LAV/HTLV-III: Fine-structure Analysis, Localization of Structural Proteins, and Detection of Envelope Antigens by Patient Sera

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LAV/HTLV-III was investigated by thin-section and immunoelectron microscopy. Formation of the virion takes place at the cell membrane. The inner components are assembled concomitant with budding, as is characteristic of type-C oncovirinae. Different from type-C viruses and typical for the subgroup of lentivirinae, these components in immature particles form an 18-nm broad, electron-dense spherical shell apposed to the viral membrane. After budding the structural components are rearranged ("maturation"). The electron-dense nucleoid formed is surrounded by a prismatic electron-opaque core shell 4–5 nm thick [1]. From immunocryoultramicrotomy, using monoclonal as well as monospecific antibodies, we concluded that the core shell is built up by p24. The inner leaflet of the envelope is covered by a 5–7-nm electron-dense layer with p18 antigenicity.

Adjacent to this layer we observed electron-dense "lateral bodies" with unknown composition and function. Knobs on the viral envelope can be demonstrated with tannic acid-treated samples. While on budding or immature particles a uniform fringe of equidistantly spaced spikes is visible, which can be labelled with anti-gp120 and/or anti-gp41 antibodies, mature virions lack these projections partially or completely. The spontaneous loss of knobs seems to be rapid. This became particularly evident when parallel cultures harvested at different times were investigated. Five- to 7-day-old cultures only rarely contained spiked particles. The knobs, about 70–80 per virion, have a height of 9 nm above the unit membrane and a diameter of 15 nm. They are connected to the virion via stalks 7–8 nm thick [2].

When patient sera were investigated by IEM it could be shown that LAV/HTLV-III-infected individuals carry antibodies directed against different viral proteins. IEM revealed a qualitative correlation of labelling intensity of viral envelope components and neutralizing capacity. The presence of antibodies in patients and the assumption that envelope proteins are also shed in vivo have important implications. First, protecting antibodies might be captured by shed proteins and are therefore not available for neutralization. Second, circulating immune complexes (CIC) can be involved in the pathogenicity of LAV/HTLV-III. CIC of unknown composition have been frequently observed in ARC and AIDS patients. An improvement of clinical symptoms after plasmapheresis of CIC has been reported [3]. The question whether LAV/HTLV-III antigens are involved in the formation of CIC can be answered by the characterization of such complexes.

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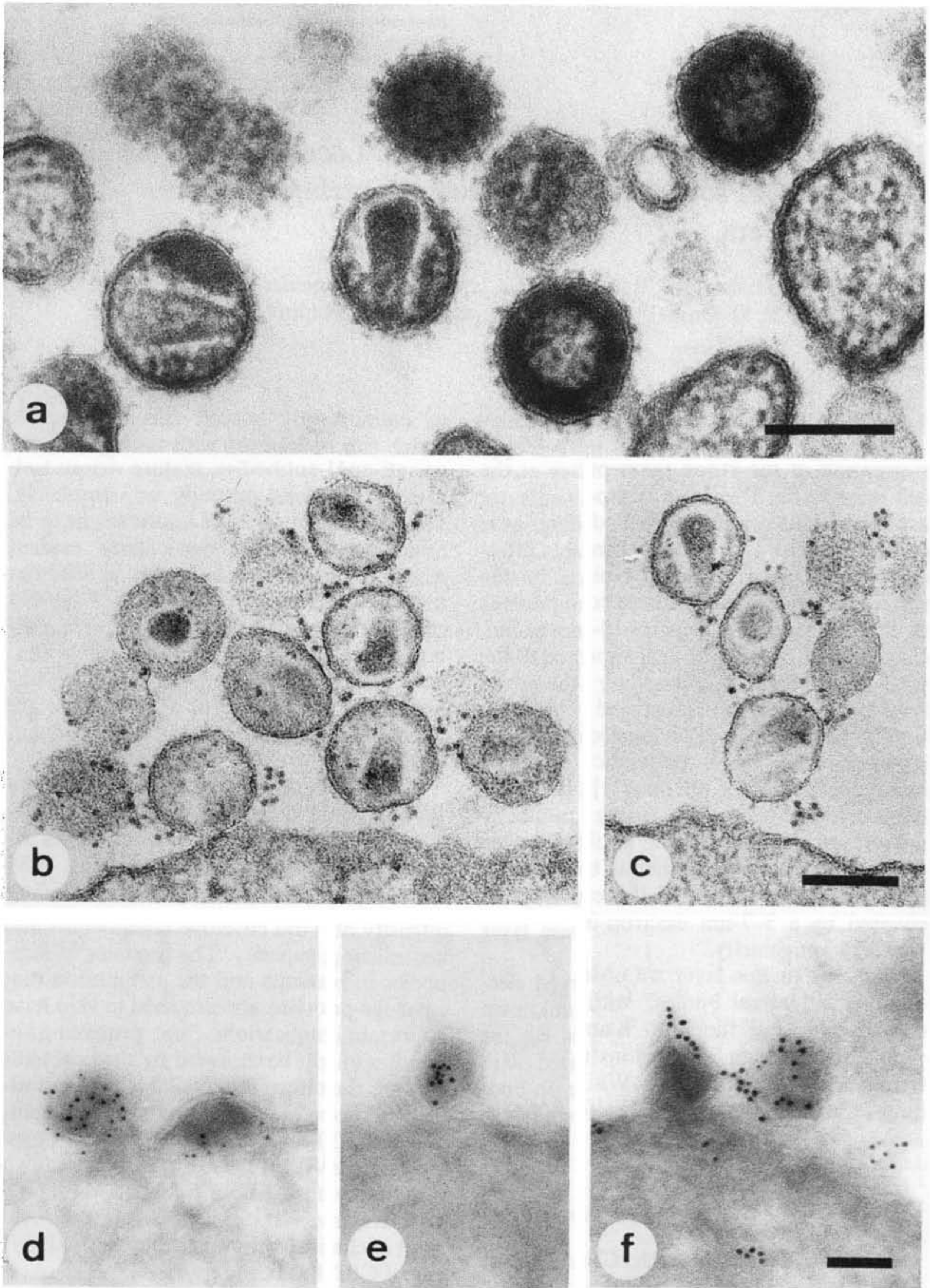

Fig. 1. a Ultrathin sections of LAV/HTLV III particles after treatment with tannic acid and Epon embedding. "Immature" particles just after budding are densely studded with knobs. The viral RNP is closely apposed to the viral membrane as a concentric shell. "Mature" particles lack the fringe of projections and show an elongated tubular core and ill-defined "lateral bodies". **b, c** Pre-embedding IEM of LAV/HTLV III using anti-gp120 (**b**) or anti-gp41 (**c**) peptide antisera. **d, e** Immuno-gold labelling of ultrathin cryosections after incubation with a p24-specific monoclonal antibody (**d**) and a monospecific anti-p24 antibody (**e**). **f** Labelling after incubation with anti-p18 hyperimmune serum leads to a shell-like distribution of the marker

References

1. Gelderblom H, Özel M, Pauli G (1985) T-Zell-spezifische Retroviren des Menschen: Vergleichende morphologische Klassifizierung und mögliche funktionelle Aspekte. Bundesgesundhbl. 28:161–171
2. Gelderblom HR, Hausmann EHS, Özel M, Pauli G, Koch MA (1987) Fine structure of human immunodeficiency virus (HIV) and immunolocalization of structural proteins. Virology 156:171–176
3. Kiprov DD, Lippert R, Sandstrom E, Jones FR, Cohen RJ, Abrams D, Busch DF (1985) Acquired immunodeficiency syndrom (AIDS)-apheris and operative risk. J Clin Apheresis 2:427–440