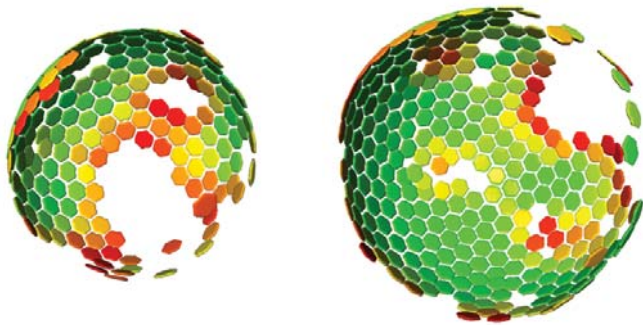


Embargoed until Monday, 22 June 2009, 23:00 BST

New electron microscopy images reveal the assembly of HIV

EMBL researchers provide the as yet closest look at the structure of immature HIV



Lattice maps for immature HIV particles. The 3D computer reconstruction shows the immature Gag lattice of HIV that matures to form the protein shell of the infectious virus. Maps are shown in perspective such that hexamers on the rear surface of the particle appear smaller. The side of the particle toward the viewer lacks ordered Gag. (John Briggs/EMBL)

Heidelberg, 22 June 2009 - Scientists at the European Molecular Biology Laboratory (EMBL) and the University Clinic Heidelberg, Germany, have produced a three-dimensional reconstruction of HIV (Human Immunodeficiency Virus), which shows the structure of the immature form of the virus at unprecedented detail. Immature HIV is a precursor of the infectious virus, which can cause AIDS. The study, published in the 22-26 June online edition of PNAS, describes how the protein coat that packages the virus' genetic material assembles in human cells. Drugs that block this assembly process and prevent the virus from maturing into its infectious form are considered a promising therapeutic approach.

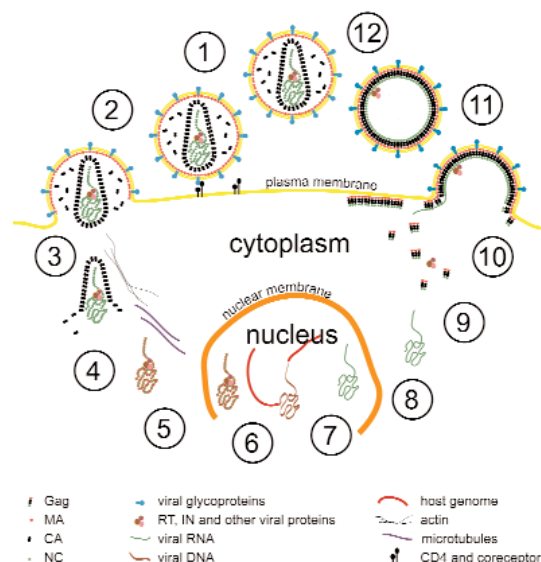
HIV consists of an RNA molecule that carries the genetic information of the virus and is surrounded by protective protein and membrane layers. During infection the virus deposits its genetic material into a human cell where it reprogrammes the host cell machinery to generate many copies of the viral genome and initiates the production of a viral protein called Gag. In the immature virus, many copies of Gag interact to form a roughly spherical lattice that encloses the virus' genetic material. The virus then leaves the cell with the help of proteins of the host and infects new cells.

Using a method called cryoelectron tomography researchers in the groups of John Briggs at EMBL and Hans-Georg Kräusslich at the University Clinic Heidelberg generated the as

yet highest resolution 3D computer reconstruction images of the immature Gag lattice. The results suggest a simple model of HIV formation in human cells: multiple Gag proteins interact to form a hexameric lattice that grows with an inherent curvature and that incorporates new proteins stochastically. Several further steps in which Gag is cleaved by an enzyme are necessary to transform this immature lattice into its mature, infectious form.

Briggs and his team are now working on producing an even higher resolution structure of the protein lattice to gain a more detailed understanding of the virus' assembly and maturation processes, which may eventually help to find weak points that could be targeted by drugs.

Cryoelectron tomography is a technique with which a sample is instantly frozen in its natural state and then examined with an electron microscope. Images are taken from different directions and assembled into an accurate 3D reconstruction by a computer. ●



A simplified representation of HIV's lifecycle. For a detailed description please refer to page 2. (John Briggs/EMBL)

Source Article

Briggs, J.A.G. et al. Structure and assembly of immature HIV. *PNAS online*, 22 June 2009

Contact:

Anna-Lynn Weaener, EMBL Press Officer, Heidelberg, Germany. Tel: +49 6221 387 452. www.embl.org. weaener@embl.de

About EMBL

The European Molecular Biology Laboratory is a basic research institute funded by public research monies from 20 member states (Austria, Belgium, Croatia, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom) and associate member state Australia. Research at EMBL is conducted by approximately 80 independent groups covering the spectrum of molecular biology. The Laboratory has five units: the main Laboratory in Heidelberg, and Outstations in Hinxton (the European Bioinformatics Institute), Grenoble, Hamburg, and Monterotondo near Rome. The cornerstones of EMBL's mission are: to perform basic research in molecular biology; to train scientists, students and visitors at all levels; to offer vital services to scientists in the member states; to develop new instruments and methods in the life sciences and to actively engage in technology transfer activities. EMBL's International PhD Programme has a student body of about 170. The Laboratory also sponsors an active Science and Society programme. Visitors from the press and public are welcome.

Simplified representation of HIV's lifecycle: The HIV lifecycle begins with the interaction of a virus particle with a receptor on the surface of a cell (step 1), which leads to fusion of the viral and cellular membranes (step 2) and deposition of the viral contents into the cell (step 3). The viral RNA genome is reverse transcribed resulting in DNA copy, which is imported into the nucleus (step 5). Within the nucleus, the viral DNA is integrated into the host cell genome (step 6). The virus may now enter a period of latency. The late stages of the viral lifecycle begin when the viral genome is transcribed from within the host genome (step 7), exported from the nucleus (step 8) and translation of the viral proteins by host cell machinery begins (step 9). The major structural protein, Gag, is transported to the plasma membrane where it directs assembly of the viral coat, and incorporates other viral proteins and the viral genome (step 10). The virus buds through the cell membrane (step 11), and Gag is cleaved by the viral protease in five places. This leads to a structural change of the virion into its mature infectious form (step 12), which is capable of fusing with a new susceptible cell.

Policy regarding use

EMBL press and picture releases including photographs, graphics, movies and videos are copyrighted by EMBL. They may be freely reprinted and distributed for non-commercial use via print, broadcast and electronic media, provided that proper attribution to authors, photographers and designers is made. High-resolution copies of the images can be downloaded from the EMBL web site: www.embl.org