Ebola virus in the World

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***Abstract*—**Ebola is a virus which potentially fatal haemorrhagic disease of humans. The virus particles are pleomorphic forms filament observed. Ebola virus genome contained 7 genes that are:L,VP24,VP30,GP,VP40,VP45و NP. Filovirus entry is mediated by the membrane glycoprotein, GP which is consists of a receptor-binding subunit, GP1, and a membrane fusion subunit, GP2.

Ebola virus haemorrhagic fever are extremely aggressive to species that infection usually results in death. It seems that the infection causes the immune system becomes impaired. Start hemorrhagic fever with symptoms such as headache , sore throat , muscle pain and symptoms such as vomiting , diarrhea , rash and shock from internal and external bleeding followed. Contact animal reservoir or direct contact with infected blood and other body fluids can spread the disease. Virus enters the host through mucosal surfaces , aerosol and scratch the skin. The largest outbreak in West Africa, which in 2013 was confirmed by the World Health Organization.So far the research , vaccine and effective treatment for this disease has not been established.

Index Terms*— *Ebola, World.

I. Prelude

The family *Filoviridae* consists of two genera, *Ebolavirus* and *Marburgvirus*, which cause a severe hemorrhagic fever in humans and in nonhuman primates [1] Within a few days, the virus induces acute fever and very often death, and is usually associated with haemorrhagic syndrome in up to 90% of symptomatic individuals.[2],[3]

Mortality rates range as high as 88%[4, 5,6). Of the four identified strains of Ebola virus, Zaire, Ivory Coast, Sudan, and Reston, the Zaire strain induces the highest death rates in humans, while the Reston strain has not caused fatal disease in humans [6],[7]. Since then Ebola outbreaks have been reported on average every 1.5 years, with a total of 7 prior outbreaks generated over 100 reported cases. A recent study has estimated 22 million people distributed in areas of Central and West Africa to be at risk of Ebola. Ebola viruses are enveloped, single-stranded, negative-sense RNA viruses.[8]

II. Structure

In their innate states, Ebola viruses exist as filamentous and pleomorphic structures, often taking on different shapes. They may occur in long filaments or branched, U-shaped, 6-shaped or circular forms0[9],[10] Ebola viruses have a uniform diameter of 80 nm but vary considerably in length, with some as long as 14,000 nm. Structurally, Ebola viruses consist of three layers: a surface glycoprotein(GP) layer, a lipid membrane envelope unit and an internal tubular helical nucleocapsid[10],[11] The outer viral envelope of the virion is derived by budding from domains of host cell membrane into which the GP spikes have been inserted during their biosynthesis. Individual GP molecules appear with spacings of about 10 nm.[citation needed] Viral proteins VP40 and VP24 are located between the envelope and the nucleocapsid (see following), in the matrix space.[12] At the center of the virion structure is the nucleocapsid, which is composed of a series of viral proteins attached to an 18–19 kb linear, negative-sense RNA without 3′-polyadenylation or 5′-capping (see following);[citation needed] the RNA is helically wound and complexed with the NP, VP35, VP30, and L proteins;[13] this helix has a diameter of 80 nm and contains a central channel of 20–30 nm in diameter.[14],[15]

III. Genome

Each virion contains one molecule of linear, single-stranded, negative-sense RNA, 18,959 to 18,961 nucleotides in length. The 3′ terminus is not polyadenylated and the 5′ end is not capped. This viral genome codes for seven structural proteins and one non-structural protein. The gene order is 3′ – leader – NP – VP35 – VP40 – GP/sGP – VP30 – VP24 – L – trailer – 5′; with the leader and trailer being non-transcribed regions, which carry important signals to control transcription, replication, and packaging of the viral genomes into new virions. [16]-[18]

These are the nucleoprotein NP encoded by the first gene [19],[20]; the polymerase cofactor P, or VP35, encoded by the second gene [21]; the viral protein VP30 encoded by the fifth gene [22]; and the major component of the polymerase complex L encoded by the seventh gene [23],[24]. The nucleocapsid proteins have a dual function in the viral replication cycle: they are involved in virus morphogenesis as structural components [25], and they catalyze replication and transcription of the RNA genome.[21]

IV. Entry

The complex steps of filovirus entry are currently being elucidated. Ebolaviruses bind to the cell surface and are internalized into endosomes, where low-pH-dependent cathepsins L and B process the heavily glycosylated GP1 into a 17- to 19-kDa protein that retains the RBD [26],[27]

There are two candidates for host cell entry proteins. The first is a cholesterol transporter protein, the host-encoded Niemann–Pick C1 (NPC1), which appears to be essential for entry of Ebola virions into the host cell and for its ultimate replication.[28],[29]. . NPC1 is a large polytopic membrane protein that resides in the late endosomes and lysosomes of all cells and is involved in transport of lysosomal cholesterol to the endoplasmic reticulum and other cellular sites [30]-[32]. While a substantial body of information about the

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housekeeping functions of NPC1 is available, its specific role in filovirus entry remains unknown. Previous findings suggest that the cholesterol transport function of NPC1 is dispensable for its viral host factor function, and that GP can bind to cellular membranes by associating directly or indirectly with full-length NPC1[33],[34] The second candidate is TIM-1 [35] The TIM family members (TIM-1, TIM-3, and TIM-4 in humans) share a type I cell surface glycoprotein structure. The ectodomains of these proteins contain an amino-terminal immunoglobulin variable (IgV)-like domain that is extended from the plasma membrane by a heavily O-linked-glycosylated mucin-like domain (MLD) [36]. In addition to serving as a receptor for filoviruses, human TIM-1 is reported to serve as a receptor for hepatitis A virus (HAV) [37],[38]

V. Disease

Ebola virus disease (EVD), previously known as Ebola haemorrhagic fever, is a highly fatal haemorrhagic fever of humans and non-human primates .[39]

The virus targets a broad range of cells, infecting monocytes, macrophages, and dendritic cells early during infection, and spreads to a variety of cell types, including epithelial cells, in the visceral organs [40],[41].

The disease course associated with Ebola hemorrhagic fever is acute and progresses rapidly. The incubation period after exposure to Ebola virus can range from 2 to 10 days. Patients often present with flu-like symptoms, such as fever, myalgia, headache, diarrhea, and vomiting. Clinical signs may progress rapidly and include severe nausea, pharyngitis, diarrhea, hematemesis, and melena. The primary routes of transmission are improper needle hygiene, direct contact with infected tissue or fluid samples, and close contact with infected patients.[42]-[45] Laboratory testing of reservoir competence shows that successful infection is possible in bats and rodents, but not in plants or arthropods.[46],[47] Ebola virus has the remarkable ability to modulate the expression of genes involved in the host immune response, causing lymphocyte apoptosis and attenuation of the protective effects of interferon.[48],[49] The host immune response is crucial and dictates the outcome of infection. Progression to severe disease occurs when the virus triggers expression of a host of pro-inflammatory cytokines, including interferons; interleukins (ILs) such as IL-2, IL- 6, IL-8, and IL-10; interferon inducible protein; and tumour necrosis factor α (TNF-α).[50],[51]

VI. Vaccine

The first indications that protective immunity could be mounted against the highly pathogenic ebolavirus arose from protection against ebolavirus challenge in rodents with inactivated viruses[52] and later with DNA vaccination.[53],[54] The final proof that a vaccine could protect primates against ebolavirus infection was obtained using a DNA vector prime, replication-defective recombinant adenovirus type 5 (rAd5) vector boost regimen, or rAd5 alone, each expressing ebolavirus glycoprotein (GP) and nucleocapsid protein (NP) in macaques.[55],[56]

Ebola virus disease licensed vaccines are still not available, but a number of vaccine approaches have been developed for Ebola virus infection in animal models, and are undergoing clinical trials. Recognising that EBOV is transmitted through wild animals such as bats, monkey and gorillas, it is recommended to avoid direct contact with bat and non-human primate blood, bodily fluids and raw meat and meat should be properly cooked before consumption.[57]

Two experimental vaccines are currently undergoing trials.[58],[59] cAd3-ZEBOV is a chimpanzee derived adenovirus vector with an Ebola virus gene inserted.[60] Trials are under way in the United Kingdom, United States, Switzerland, and some African countries. rVSVZEBOV is an attenuated vesicular stomatitis virus with one of its genes replaced by an Ebola virus gene. Human trials have started in the US.[61]Results for the VSV-EBOV vaccine trial in Guinea published in July 2015 showed promise.[62],[63]

VII. Epidemiology

The first Ebola virus disease (EVD) outbreak occurred simultaneously in Nzara, Sudan (involving 281 patients out of which 151 died [54%]) [64] and Yambuku, Zaire (now the Democratic Republic of Congo) (involving 318 patients out of which 280 died [88%]) [65]in 1976. The disease got its name from the Ebola River, which passes near the Yambuku village where the outbreak first occurred [66] The first case of the current EVD outbreak in West Africa was reported in Guinea in March 2014 [67] and from there it spread across land borders to Liberia and Sierra Leone, and to Senegal (by land travel) and Nigeria (by air travel) [68],[69]. The World Health Organization (WHO) declared it a "Public Health Emergency of International Concern" on August 7, 2014 [69] Viral sequence of Ebola patients in Sierra Leone showed that the epidemic was originated from sustained person-to-person transmission without additional introductions from animal reservoirs. Its case-fatality rate has been estimated approximately 70%. (70)In Liberia and Sierra Leone, the magnitude of the outbreak was not clearly underestimated because of individuals with Ebola virus disease being cared for outside the hospital setting. Accumulative number of presumable, suspected, and laboratory-confirmed case of Ebola virus is 19,065 including 7,388 deaths as of December 17, 2014.[69] Our findings show that the protocol used in our study to diagnose rabies was effective and applied method.

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