Chapter 7

Ebola Virus's Glycoproteins and Entry Mechanism

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Additional information is available at the end of the chapter

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Abstract

Ebola virus glycoprotein (GP) is the only protein that is expressed on the surface of the virus. The GP proteins play critical roles in the entry of virus into cell and in the evasion of the immune system. The GP gene transcript to membrane GP is constituted of two subunits GP1 and GP2,and the secretory GP (sGP). The main function of GP1/2 is to attach virus to target cell's membrane, whereas sGP has multiple functions on Ebola pathogenesis, such as inactivate neutrophils through CD16b causing lymphocyte apoptosis and vascular dysregulation. There are many studies that focused on better understanding the GP mechanism and aim at developing new antibodies and drugs such as VSV-EBOV, cAd3-EBO Z, rVSVN4CT1 VesiculoVax, 'C-peptide' based on the GP2 C-heptad repeat region (CHR) targeted to endosomes (Tat-Ebo) and MBX2270. In this chapter, we discuss the Ebola viral glycoproteins, genomic organization, synthesis, and their roles and functions. On the other hand, we treat the mechanisms of pathogenicity associated with Ebola GPs.

Keywords: EBOLA, virus, glycoprotein (GP), entry, mechanism, pathogenesis, structure

1. Introduction

Since the beginning of the year 2012, cases of Ebola virus have been reported in four African countries: Guinea, Liberia, Sierra Leone and Nigeria. WHO announced the end of Ebola outbreak in January 2016 [1]; despite this, according to the WHO, new cases are declared later in Sierra Leone, Liberia and Guinea [2, 3]. What this highlights is that the risk of the Ebola

epidemic is still standing. The Ebola haemorrhagic fever weans and is often fatal in humans. It is caused by *Filoviridae*, citing the species Zaire Ebola virus (ZEBOV).

Ebola virus is a pathogenic agent of Ebola haemorrhagic fever; it is a single-stranded RNA with negative sense and with a genome length of approximately 18,920 nucleotides. Since it belongs to *Filoviridae*, its diameter is about 80 nm with a twisted filamentous form. Generally, the virus length is up to 1.1 μm [4], but particles of 14 μm were detected in the culture of liver tissue [5]. The viral RNA contains information about eight proteins, VP24, VP30, VP35, VP40, L, NP, sGP and GP1/2. Each of the protein expressed by EBOV is known for its multi-functionality that is why it is nominated as Swiss Army Knife, essentially VP35 and GP that present multi-functionality in the pathogenesis process and in the inhibition of immune responses in the host. EBOV is classified as a Category A priority pathogen by the National Institute of Allergy and Infectious Diseases (NIAID) and a Category A agent of bioterrorism by the Centers of Disease Control and Prevention (CDC) [6].

The principal characteristics of the Ebola virus is the presence of a heavily glycosylated GP on the external surface of viral membrane. Crystallographic studies revealed that GP on the viral surface exists in the trimeric form [7].

This chapter aims to provide a current overview on the treatment of GP of the Ebola virus, genomic organization, synthesis, their roles and functions, and the mechanisms of viral entry associated with GP and replication.

2. Phylogenetic information of Ebola virus

A total of 132 sequences are collected from the NCBI gene database. The samples were collected from the Makona river (80 sequences from Sierra Leon and 52 from Guinea), and they were collected in the period between 1 June 2014 and 30 August 2015. They underwent a global alignment and phylogenetic analysis by MEGA 6.4 and BEAST [8, 9].

Phylogenetic analysis reveals a greater genetic diversity with the presence of three distinct lines. The first line represents a set of sequences found only in Guinea, and that is most closely

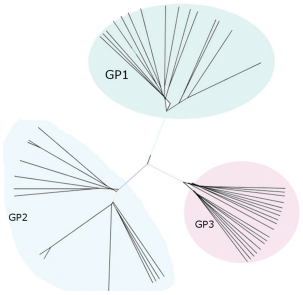

Figure 1. Phylogram of Ebola virus obtained with BEAST, the phylogenic software based on Bayesian evolutionary analysis. The first cluster (GP1) contains sequences from Guinea alone. In second cluster (GP2), we may find sequences from Sierra Leone and Guinea. In third cluster (GP3), the sequences from Fore'cariah, Dalaba are collected.

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