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Identification of active pocket and protein druggability within envelope glycoprotein GP2 from Ebola virus

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ABSTRACT

The drug searching for combating the present outbreak of Ebola virus infection is the urgent activity at present. Finding the new effective drug at present must base on the molecular analysis of the pathogenic virus. The in-depth analysis of the viral protein to find the binding site, active pocket is needed. Here, the authors analyzed the envelope glycoprotein GP2 from Ebola virus. Identification of active pocket and protein druggability within envelope glycoprotein GP2 from Ebola virus was done. According to this assessment, 7 active pockets with varied druggability could be identified.

1. Introduction

In year 2014, the most serious Ebola outbreak in Africa and becomes the present global threat. Thousands of Africans get infected and there are many death cases. The drug searching for combating the present outbreak of Ebola virus infection is the urgent activity at present[1]. World Health Organization declares and calls for international collaboration for fighting the big outbreak of Ebola virus in Africa[2,3]. Finding a new effective drug at present must base on the molecular analysis of the pathogenic virus. The in-depth analysis of the viral protein to find the binding site, active pocket is needed[4]. This can be done by a complex crystallography study. With the advent of bioinformatics technology at present, it is possible to further manipulate on the crystallography data of the focused viral protein. The druggability within the identified active pocket can be further analyzed.

2. Materials and methods

The authors firstly searched for the crystallography data of envelope glycoprotein GP2 from Ebola virus. The public available data, PubMed, was used as the basic search tool. The derived "Core Structure Of GP2 From Ebola Virus [Envelope Glycoprotein]" from Ebola virus- Mayinga, Zaire, 1976 was used as the primary template for further analysis of protein active pocket and druggability. To analyze for protein active pocket and druggability, the standard bioinformatics technology was used. DoGSiteScorer

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was the main tool for analysis[5].

3. Results

According to the search, the standard referenced Protein Data Bank crystal structure of the envelope glycoprotein GP2 from Ebola virus could be derived and used for further manipulation. According to the analysis, there are 7 identified active pockets within the studied molecules with druggability ranging from 0.25 to 0.73 (Table 1).

Table 1

Identified active pocket and corresponding druggability (listed by volume from the most to the least).

Identified pockets	Area (Angstrom3)	Volume (Angstrom2)	Drug score
1	986.23	345.66	0.67
2	385.20	309.57	0.73
3	456.43	294.27	0.59
4	351.14	175.36	0.39
5	237.39	173.25	0.37
6	100.72	144.51	0.41
7	353.67	128.96	0.25

4. Discussion

The success for control of the present outbreak of Ebola virus 2014 might be depended on two main thing: drug and vaccine[1]. To search for new drugs, we need the complete knowledge on the viral protein structure and the interrelation to possible new drugs. Identification on the active pocket, which can be the binding site to newly developed drug is needed[6]. Here, the authors studied the important molecule, envelope glycoprotein GP2 from Ebola virus. The technique use in this study is the standard technique used in many recent studies[7,8].

In fact, envelope glycoprotein GP2 from Ebola virus is the well-known target for trial for control of the Ebola virus. This protein plays an important role in cell invasion of virus[9], hence, if there is any new drug attacking this protein, it will be a good drug for fighting the virus, preventing it from cellular entry[10]. In this work, the authors use the referencing bioinformatics method for assessment of active pocket and druggability within envelope glycoprotein GP2[11]. It is successful to identify 7 pockets with can be selectable for further development of the new drug for targeting of drug binding to those active pocket. Selection of the active pocket with large size and high drug score to be the first focused target is suggested.

Conflict of interest statement

We declare that we have no conflict of interest.

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