



SDI Review Form 1.6

Journal Name:	British Microbiology Research Journal
Manuscript Number:	2015_BMRJ_16297
Title of the Manuscript:	Descriptive analysis of Ebolavirus proteins: towards development of effective therapies
Type of the Article	Review Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



SDI Review Form 1.6

PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	Major: on first glance, the content of this review appears scientifically accurate. However, the referencing of this manuscript is abysmal, making it impossible to verify whether the described science is correctly interpreted. I therefore made it only to page 4 before I gave up reviewing the paper further. I would be willing to actually review the entire paper once this issue and the other issues mentioned below are carefully addressed. In terms of references, for instance: - line 51: reference 2 is not a primary reference to fruit bats or chimps - line 55: references 3-14 are a concoction of reviews and articles, none of which are primary references for BSL-4 classification (that should be a reference to the BMBL 5th edition), the simultaneous outbreaks in Zaire and Sudan (those should be the Bull WHO papers of 1976) etc. - Line 59: reference 8 addresses clinics and pathology and not the statement about the current virus being an "outlier" (which is a misinterpretation). The reference should be the Baize et al. NEJM paper on the genomic characterization of the current virus	Thank you so much for raising your concerns about our manuscript. You motivated us to improve the manuscript. We hope that you will be able to review our revised manuscript. Your valued comments and suggestions will be much appreciated. Primary references for fruit bats have been used in the revised manuscript. See line 48 (reference 4). The statement about chimps was deleted as it was misleading indeed. Thank you. We agree with you. We have deleted the whole segment about BSL-4 including references 3-14 and line 55. The word "outlier" together with the whole sentence has been deleted. It was not adding value to the article. Reference 8 was removed. The introduction has been re-written.



SDI Review Form 1.6

	- Line 93: references 2 and 17 are reviews on pathogenesis and vaccine papers rather than taxonomy papers that should be cited here. - Line 95: The family <i>Filoviridae</i> and the etymology of filum was published by Kiley in Intervirology; reference 2 should be replaced with that - Line 97 and 98: reference 28 is a paper on N glycans, not on taxonomy/ebolavirus diversity - Line 102: the first paper on the genome of Ebola virus should be cited here! - Reference 2 and 10 should be replaced with primary papers describing the structure of filovirions - Line 140: reference 32 is a taxonomy paper, rather than a primary reference on the NP protein! - Etc. etc. It appears to me that somebody compiled information on ebolaviruses from all sources available and then retrospectively inserted random references behind statements. Less major: - Line 6: "up to 90%" is misleading. There have been outbreaks with 100%. The authors should use the mean CFR of all outbreaks, which is currently around 40% (and the authors should be clear whether they refer to EVD outbreaks caused by Ebola virus, or by EVD caused by all four ebolaviruses that can cause it)	Thank you. We are grateful for noticing the error. Proper taxonomy papers have since been cited. See line 67-74 and Table 1 and reference 9,10 Agreed. We have used latest primary references on taxonomy, (see ref. 9,10) The section describing the structure and classification of Ebola viruses has been re-written as suggested. See line 65-88. We have inserted Table 1 to show the latest taxonomy of filoviruses. Only primary articles on virus structure and taxonomy have been cited (see ref. 2, 7, 8,9,10 11, 12). Citations from review articles have been removed. We got it wrong the first time but we have addressed your valuable concerns on references We have removed the whole segment and replaced it with recent data on EVD from West Africa. See line 31-34 and reference 1. Care has been taken throughout the document to mention specific viruses
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SDI Review Form 1.6

	- Line 22-23: who says that siRNAs are the best options for treating EVD? This is not the current view of WHO, CDC, MSF, who only list siRNAs among various promising options. This article should not endorse a product. - Line 29 and elsewhere: should be “EVD survivors”. Ebola is a river, Ebola survivors would be people who did not drown after falling in... The authors should carefully edit the manuscript and use “Ebola virus” or “ebolavirus” and “Ebola virus disease” instead of “Ebola”. Only EVD breaks out; viruses do not. - Line 42-43: “the mechanisms devised by bats”: please delete: as no bat infectious are known this has to be pure speculation. But then I also did not find the announced discussion in the paper. - Line 50-51: no. It is currently often repeated that bats are the hosts, but there is very little evidence and the authors should point that out. No infectious Ebola virus has ever been isolated from a bat, nor have complete genomes been detected in any of these animals. Likewise, the gorilla and chimp connection is dubious. Only one ebolavirus, Tai Forest virus, has been associated directly with chimpanzees. - The nomenclature used in the manuscript is outdated. Line 92 forward and elsewhere: “marburgviruses”, “cuevaviruses” and “ebolaviruses” should not be capitalized; MARV is NOT the abbreviation for “marburgviruses” (of which there are two), but for one of them, which is called “Marburg	We agree with you. The statement was incorrect and we have deleted it. The revised manuscript has avoided endorsing products We have rectified it throughout the revised manuscript. See line 174, 491, 532, 591. We have used EVD through the revised manuscript, see line 12, 21, 31, 50, 59, 369, 372, 459, 684 etc. The statement, “the mechanisms devised by bats”, was deleted and the whole section was rephrased. See line 60-64. Bats are discussed under future perspectives, see line 660-681 This has been corrected and the lack of evidence has also been emphasised. See line 47-51. Thank you. Agreed. The nomenclature was outdated indeed. We have updated the nomenclature, see line 67-78 and Table 1. Line 92 was describing genera of filoviruses thus, capitalisation of “<i>Marburgvirus</i>”, “<i>Cuevavirus</i>” and “<i>Ebolavirus</i>” is supposed to be correct, See Table 1 and ref. 9, 10. We have agreed to remove MARV. Thank you so much.
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SDI Review Form 1.6

	virus". <i>Filoviridae</i> ought to be capitalized. All virus names and abbreviations are outdated/wrong: should be Ebola virus (EBOV), Sudan virus (SUDV), Reston virus (RESTV), Tai Forest virus (TAFV), and Bundibugyo virus (BDBV). "Zaire Ebolavirus" should be "Ebola virus" throughout; there are no subtypes, but five distinct ebolaviruses (with Ebola virus being one of those five). EBOV is NOT the abbreviation for "Ebolavirus", but for "Ebola virus" (note the space). "<i>Ebolavirus</i>" refers to a genus (and the name should be italicized); there are five ebolaviruses. The word "species" should not be used anywhere, as species are concepts of the mind and do not have proteins. Instead species are represented by viruses. Etc. etc. The authors should carefully review the many recent publications on correct and up-to-date filovirus taxonomy, most of which are open-access. - Line 57-59: this sentence doesn't make any sense. The current Ebola virus variant (Makona) is of course homologous to other previous Ebola virus variants as otherwise it would not be Ebola virus (and it should be "variant", not "subtype" – also elsewhere) - Line 60: rodents??? This has been abandoned over ten years ago. - Line 63: natural filovirus variants are never strains based on the latest definitions by the ICTV <i>Filoviridae</i> Study Group - Line 68 and elsewhere: the disease is called "Ebola virus disease (EVD). Therefore it should be "EVD patients"	<i>Filoviridae</i> has been capitalised. See line 68, 73 Correct abbreviations for Ebola virus have been inserted, see Table 1, line 76-77 The valuable information is appreciated. We rectified the problem of abbreviations throughout the revised manuscript See Table 1. We have carefully avoided the use of the word, "species". This has been done as seen with the use of more recent references by Kuhn et al (see ref. 9, 10). Thank you. We agree. Line 57-59 has been deleted. Thank you so much for the correction. Line 60 has been deleted Corrected and line 63 has been deleted Noted. We have rectified this problem throughout the revised manuscript. See line 12, 21, 31, 50, 59, 369, 372, 459, 684
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SDI Review Form 1.6

	- Throughout: the N and O and “N-linked” and “O-linked” ought to italicized throughout - - Line 216: the crystal structure of GP clearly demonstrated that the receptor-binding regions is NOT a domain. Other: The manuscript needs to be carefully edited for language by a native English editor. Spaces and periods are missing between words throughout the text and the grammar is often all over the place. The text needs more precision. Ethical issue: Yes – the referencing is abysmal and highly unfair to the scientists who performed experiments and reported results initially.	<i>N-linked and O-linked</i> have been italicised. See line 106-107, 125, and 134. Thank you. However, I could not find a paper that shows that receptor binding region is not a domain. I would be happy to read that paper. We have strived to correct Syntax and grammar throughout the revised manuscript. A native English speaker went through the manuscript and his comments were taken care of. Referencing has been carefully addressed with focus on primary refs and citations from reviews were deleted.
Minor REVISION comments		
Optional/General comments		Thank you for reviewing our manuscript. We really appreciate your input.