Reviewer’s report

Title: The Site of Exposure May Influence the Time of Virus Appearance in the Blood and Virus-Specific Immune Responses in Primary SIVmac251 Infection of Rhesus Macaques

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Reviewer: Dr Anil Kumar

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Accept without revision

The manuscript entitled 'The site of exposure may influence the time of virus appearance in the blood and virus-specific immune responses in primary SIVMAC251 infection' by Stevceva and co-workers describes emergence of virus in the blood and development of virus-specific cellular immune responses in two rhesus macaques that were inoculated with same SIVMAC251 stock by two different routes. They infected two rhesus macaques, one by intravenous inoculation of the virus whereas other animal was infected by intrarectal route. The viral RNA was detected earlier in the animal that was infected by intravenous route. However CD4 T cells loss remained comparable in both animals. This was accompanied by reverse pattern in the emergence of virus-specific CD8+ T cell responses. The animal inoculated by intrarectal route developed virus-specific immune cells within 4 days after infection whereas virus-specific CD8+ T cells became detectable only 12 days after intravenous exposure in the other macaque. On the contrary magnitude of cellular responses was higher in the macaque that was infected by intravenous route. This manuscript provides some interesting original information regarding effect of different routes of exposure on in vivo virus replication and development of specific immune responses. Furthermore use of ultra sensitive tetramer technology provides in depth and accurate information regarding kinetics of Env, Gag and Tat-specific CD8+ T cells. Given the small number of animals used in this study, it is difficult to draw definite conclusion. However I fully concur with the authors that consequences of this study, if confirmed in studies with larger number animals, may have unequivocal implications for vaccine development.

The work is original and timely. The people involved in virology research especially those involved in vaccine design will find this report very useful for their future work and I strongly recommend this manuscript for publication.

Minor comments:
1. Page-9, Line-8: Table number should be provided.
2. Please provide heading for Table-1.

**Competing interests:**

None declared.