



## REPLY TO ZAHEDNASAB ET AL.: HHV-6 and marmoset EAE

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We thank Zahednasab et al. (1) for their enthusiastic support of our paper (2) and insightful comments. We wholeheartedly agree that additional studies are needed to more fully elucidate mechanisms underlying the association of HHV-6 and other viruses with neuroinflammatory pathologies like multiple sclerosis (MS).

The authors correctly note that in many rodent models of experimental autoimmune encephalomyelitis (EAE), the spinal cord is predominantly affected. However, in marmoset EAE, both brain and spinal cord are affected (3, 4). In our ongoing studies, we are using a combined MRI–histopathological approach to characterize the spectrum of spinal cord lesions in marmoset EAE, which further underscores the relevance of this non-human primate model to MS.

We agree that EAE ranking scales are quite useful in standardizing disease course across studies. The EAE ranking scale (0 to 3) used in our study is detailed in the materials and methods section of our paper (2).

Due to manuscript space constraints, we were unable to include all of the data collected during our study. Because a clinical score of 3 was a predefined clinical end point, the survival curve in figure 2A of ref. 2 represents the time when marmosets reached this end point. Indeed, we have been evaluating a more comprehensive clinical scale for marmoset EAE based on a pediatric neurologic examination performed by a trained neurologist.

As with any nonhuman primate study, we strive to minimize the number of animals per group, which may affect statistical outcomes. Given that we included only four animals per group, a *P* value of 0.05 following a comparison across groups suggested to us that the greater fraction of T1 lesion burden in the HHV6B group was worth discussing.

Finally, we agree with Zahednasab et al. (1) that further studies are warranted to elucidate the precise mechanism of HHV-6 in the pathogenesis of MS.

- 1 Zahednasab H, Keyvani H, Karampour S, Harirchian MH (2018) Role of HHV-6 subtypes in accelerating EAE progression. *Proc Natl Acad Sci USA* 115:E12126.
- 2 Leibovitch EC, et al. (2018) Herpesvirus trigger accelerates neuroinflammation in a nonhuman primate model of multiple sclerosis. *Proc Natl Acad Sci USA* 115:11292–11297.
- 3 Absinta M, Sati P, Reich DS (2016) Advanced MRI and staging of multiple sclerosis lesions. *Nat Rev Neurol* 12:358–368.
- 4 Maggi P, Sati P, Massacesi L (2017) Magnetic resonance imaging of experimental autoimmune encephalomyelitis in the common marmoset. *J Neuroimmunol* 304:86–92.

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The authors declare no conflict of interest.

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