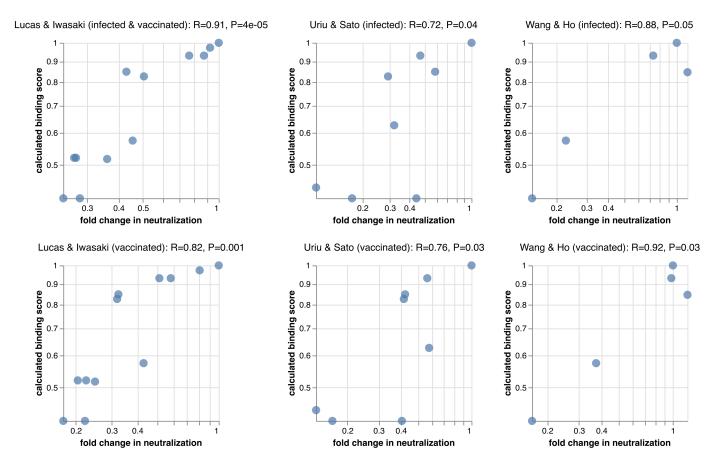
## **Supplementary Material**



**Figure S1** A version of Figure 3 where the estimations are made using the mean effects of tolerated mutations at a site rather than the total (sum) of the effects of tolerated mutations at a site. The results are almost identical.