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Review of: "Influenza A virus reassortment in mammals gives rise to genetically distinct within-host sub-populations"

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The authors tried to answer the question of how viral population structure within hosts such as guinea pigs, ferrets and pigs shaped genotype diversity generated through reassortment. They monitored reassortment by co-infected animals with wild type and synonymously barcoded variant viruses of a pandemic H1N1 strain background and thus in the absence of selection pressure.

The results presented showed that co-infection at the cellular level is extensive and reassortant viruses are consistently observed in both the upper and lower respiratory tracts throughout the course of infection. Also, viral populations in the upper and lower respiratory tract are genetically very different, revealing strong spatial compartmentalization. The authors emphasize that the spatial structure within the mammalian respiratory tract is a major factors in determining the extent of influenza virus diversity engendered through reassortment.

This study showed that the genetic diversity of influenza virus in swine is generally lower than in guinea pigs and ferrets. However, when using highly similar parental viruses it can be assumed that they are recognized as one virus by the host. In that case, the reassortment is more of a random process like in the viral quasispecies evolution concept. Therefore, when two different viruses are used, the frequency of reassortment in these hosts may differ from the results obtained in this study. It is worth mentioning that during influenza A virus assembly, all eight separate viral RNA segments are incorporated into virions in a selective manner. It has been suggested that influenza A virus packaging signals play a critical role in mediating the reassortment between different viruses. Also, it has been indicated that in natural or experimental competitive situations, the number of reassortants was very low, and the genotypes were not random.[1]

Overall, the article is well-organized, with the methodology clearly explained and the results well presented. Only the stacked plots (Fig. 1 and Supp. Fig. 1) could be improved by changing the background from blue to white. Blue is also used to represent the results of the wild type strain, therefore the blue background makes it difficult to analyse the graphs.

[1] Li X, Gu M, Zheng Q, Gao R, Liu X.: Packaging signal of influenza A virus. Virol J. 2021;18:36. doi: 10.1186/s12985-021-01504-4.