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Oral presentation

OA06-02. Monospecific expansion of SIVmac251 during acute infection masks multiple transmitted virus variants revealed during the chronic phase

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Background

Rhesus macaque challenge models to evaluate protection are important in the search for an AIDS vaccine. Many challenge protocols use high dose SIV to ensure infection of all control animals after a single challenge. Many virus variants are predicted to infect the animals under these conditions, which is different than the majority of human infections. It is important to identify both the infecting virus swarm in the stock, and the transmitted and replicating virus, to better evaluate vaccine candidates. It is important to develop macaque models predicting human vaccination outcome.

Methods

We performed single genome amplification (SGA) to identify the full env sequence or a fragment encompassing the highly variable V1/V2 region from naive SIVmac251-challenged animals using plasma from the acute and chronic phase, as well as from the original SIVmac251 challenge stocks.

Results

The two closely related SIVmac251 stocks sequenced by SGA showed great diversity of env sequences. Most changes were within the V1/V2 region, known to be immunodominant for SIV antibody responses. Despite the stock diversity, only a very narrow selection of similar envs were detected during the acute phase in 7 of 9 animals infected by atraumatic mucosal application. In contrast, multiple diverse env sequences were found in the chronic phase, which can be traced back to the stock.

Conclusion

Multiple species cross the mucosal barrier and infect the host during a high dose mucosal infection. Interestingly, one or very few of these variants propagate early in the acute phase, but other transmitted variants emerge to prominence later. This may be the result of viral fitness, competition, founder effects, or innate mechanisms. These findings also suggest that estimating the number of transmitted virus variants by analysis during the acute phase is inaccurate, and evaluation of both acute and chronic virus is critical to identify the transmitted variants.