Reply to “Control of Simian Immunodeficiency Virus SIVmnd-1 RNA Plasma Viremia after Coinfection or Superinfection with SIVmnd-1 in SIVmnd-2-Infected Mandrills and Vice Versa”

In their comment on our article, Liégeois et al. raise two important discussion points. First, they provide new and interesting viral load (VL) data from infected mandrills in the Centre International de Recherches Médicales de Franceville (CIRMF) semi-free colony. By showing that in SIVmnd-1 and -2 dually infected mandrills, the levels of SIVmnd-1 RNA are always lower than in SIVmnd-1 singly infected animals, they confirm in a larger group of mandrills our previous observation. Second, they report that a very active transmission of simian immunodeficiency virus (SIV) (mainly involving SIVmnd-1) occurred recently in the colony.

For plasma VL quantification, Liégeois et al. optimized a new real-time reverse transcription (RT)-PCR assay that employs specific probes for either SIVmnd-1 or SIVmnd-2 and an external reference plasmid. As described in reference 6, for our study, which was conducted in 2004, we used a real-time SYBR RT-PCR assay targeting the same region and an external synthetic RNA standard that enabled us to quantify at a cutoff of 250 copies/ml plasma for both SIVmnd-1 and SIVmnd-2 (6). (In the assay by Liégeois et al., the limit of detection is 310 copies/ml plasma.) During the optimization process, we calibrated the assay using culture supernatants and showed that quantification was optimal and independent for each virus in culture media containing the two viruses. Therefore, our approach is very similar to that described by Liégeois et al. We also noticed that in dually infected mandrills, SIVmnd-2 tends to be the major replicative form. For the sake of simplicity, we did not detail these data in our original paper. Moreover, during the long-term follow-up of superinfected mandrills, the SIV viral load is consistently high, but SIVmnd-1 shows a tendency to replicate at lower levels than SIVmnd-2 (Fig. 1). Interestingly, as shown in our paper, the overall VLs during the initial stage of dual SIVmnd-1 and -2 infection are in the same range as those observed in singly infected mandrills (10^6 to 10^6 SIVmnd RNA copies/ml), even when taking into account both viruses. Later in the infection, however, the VLs are consistently higher, although not significantly (Wilcoxon’s rank test).

In our study conducted in 2004, we included all 23 SIVmnd-infected mandrills housed in CIRMF, except those who were too young to be sampled (i.e., <3 years of age). Only three of our sampled animals were below 5 years of age. Notably, according to the data provided by Liégeois et al., the number of infected mandrills has more than doubled since our study, with 33 new SIVmnd-1 infections and the first documentation of a natural SIVmnd superinfection. Such a rapid spread of the SIVmnd in the CIRMF colony is unprecedented. Indeed, during the 20 years of follow-up prior to 2004, very limited transmission of either type of SIVmnd occurred: SIVmnd-2 was transmitted between four males (5) during their fight for sexual dominance (2, 4) and was likely absent from the colony from 1995 (the time of the demise of the last of the four SIVmnd-2-infected males) until 2004. Similarly, SIVmnd-1 spread was also limited to a few cases of mother-to-infant transmission. This limited spread of the two viruses was likely related to the management of the CIRMF colony, with the SIV-infected mandrills kept in a specific enclosure to avoid large intracolony transmission to uninfected mandrills and animals being sampled and tested every year (1, 3, 7). Furthermore, the dually infected animals were part of experimental protocols and thus were housed in single cages to allow more intense sampling and clinical follow-up. At the completion of the project (2004), the animals were reintroduced into a “superinfected” semi-free enclosure, according to the Institutional Animal Care and Use Committee (IACUC) protocols of these experiments.

The observation of a rapid and massive nonexperimental transmission of SIVmnd in the CIRMF colony of mandrills demonstrates a nice opportunity for a closer follow-up of nonhuman primate colonies housing SIV-infected and uninfected animals for AIDS research-related purposes.

REFERENCES


Address correspondence to Pierre Roques, pierre.roques@cea.fr.

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Sandrine Souquiere  
Centre International de Recherches Médicales de Franceville (CIRMF)  
Franceville, Gabon

Cristian Apetrei  
Center for Vaccine Research  
University of Pittsburgh  
Pittsburgh, Pennsylvania, USA

Ann Chahroudi  
Yerkes National Primate Research Center  
Emory University  
Atlanta, Georgia, USA

Ivona Pandrea  
Center for Vaccine Research  
University of Pittsburgh  
Pittsburgh, Pennsylvania, USA

Guido Silvestri  
Yerkes National Primate Center  
Emory University  
Atlanta, Georgia, USA

Pierre Roques  
Institute of Emerging Diseases and Innovative Therapies  
CEA  
Fontenay-aux-Roses, France