Modeling viral kinetics predicts a rapid establishment of the cytotoxic immune response targeting distinct infected cell compartments in SIV controller macaques

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**Objectives**: Long term control of SIV can be obtained in cynomolgus macaques presenting a H6 MHC allele or in non-H6 animals infected with a low inoculum of SIVmac251 by mucosal route. Here we aimed to characterize the viral kinetics in this model, in order to better understand the determinants of viral control.

**Methods**: The kinetics of SIV RNA and SIV DNA was obtained for 18 months in 16 macaques. SIV RNA and DNA data were jointly fitted with a mechanistic model of viral infection, using nonlinear mixed effect models (SAEM algorithm, implemented in Monolix).

**Results**: No differences were found in the acute infection, but controllers tended to have a more rapid viral decline after the peak, which could be best reproduced assuming a cytotoxic immune response with a saturable infected cells-dependent growth rate. In this model viral control did not correlate with the strength of the immune response \textit{per se}, but rather with the ability to rapidly establish an effective response after peak viremia. Best simultaneous fit to RNA and DNA kinetics was obtained assuming 3 compartments of infected cells: actively infected cells with a short half-life decreasing from 5.5 days to 0.3 days after peak viremia, and two populations of non actively infected cells, with half-life of 5.1 and 118 days. In controllers at setpoint, these populations account respectively for less than 1\%, around 5\% and more than 90\% of circulating infected cells (Figure 1).

**Conclusions**: Modeling predicts that an early establishment of an effective CD8 response is key to achieve viral control. Discrepancy between SIV-RNA and SIV-DNA kinetics reveals that most of SIV-DNA containing cells are not highly producing and not highly targeted by the immune response in these controllers.

The results in this abstract will be previously presented at IAS 2017.