



**Extended Data Figure 8 | Analysis of cytokine expression and release after activation of TLR-4.** **a**, TNF release from whole blood upon stimulation with lipid-A. Whole blood was stimulated with lipid-A at the indicated concentrations for 4 h and cytokine secretion was measured by cytometric bead array.  $n = 5$  biologically independent samples for *M. mulatta*;  $n = 4$  biologically independent samples for *C. atys*. **b**, IL-6 release from whole blood upon stimulation with lipid-A. Whole blood was stimulated with lipid-A at the indicated concentrations for 4 h and cytokine secretion was measured by cytometric bead array.  $n = 8$  biologically independent samples for *M. mulatta*;  $n = 9$  biologically independent samples for *C. atys*. **c**, SIV<sub>smm</sub> plasma viral load for *M. mulatta* and *C. atys*. SIV<sub>smm</sub> RNA levels in plasma were quantified at the indicated time points after intravenous inoculation with a primary uncloned SIV<sub>smm</sub> *C. atys* isolate.  $n = 5$  biologically independent samples for each species. **d**, *TLR4* mRNA levels in LPS-stimulated blood samples. To test the level of *TLR4* expression in the LPS-stimulated blood samples shown in Fig. 3e, we isolated RNA from whole blood from time-point

matched replicate samples using PAXgene Blood RNA tubes, and analysed expression using Affymetrix GeneChip Rhesus Macaque Genome Arrays, which contains three independent probesets specific for *MmTLR4* (denoted on the x axis). Probeset intensities are displayed along the y axis as RMA normalized values.  $n = 3$  biologically independent samples for *M. mulatta*;  $n = 4$  biologically independent samples for *C. atys*. **a–d**, Dots represent individual animals, and the bar represents the mean. Unpaired two-sided Student's *t*-test, *P* values are indicated. **e**, *TNF* and *IL6* mRNA levels in LPS-stimulated monocytes from *M. mulatta* and *C. atys*. RNA-seq was used to assay global changes in gene expression after LPS stimulation of primary CD14<sup>+</sup> monocytes. Significance for comparisons of mRNA levels of individual genes was tested using the Wald test as part of the DESeq2 workflow. Bars represent group means, and dots represent read counts for individual samples normalized to library size. Indicated *P* values are adjusted using the Benjamini–Hochberg correction.  $n = 6$  biologically independent samples for each species.