SUPPLEMENTARY MATERIAL

Table S1. Nucleotide changes in SIVmac optimized sequence.
The table shows nucleotide in WT sequence (upper line) and optimized sequence (left column). Numbers are mutations between each sequence.

From / To	**A**	**C**	**G**	**T**
A		1	0	6
C	160		31	45
G	54	0		20
T	30	0	11	

Table S2: Mutations observed in SIVopt1, SIVopt2 and SIVwt genomic sequences after 10 weeks of culture in Cemx174. The genomes of passaged viruses were fully sequenced and their consensus sequences were compared to their original sequences before passaging.

	Mutation	Position*	Gene	WT/Opt region	Amino acid change
SIVwt	T->A	405	5' LTR	WT	Non coding
	T->C	829	5' LTR	WT	Non coding
	G->A	1782	Gag (CA)	WT	Asp->Asn
SIVopt1	T->C	693	5' LTR	WT	Non coding
	G->A	706	5' LTR	WT	Non coding
	A->G	752	5' LTR	WT	Non coding
	T->C	829	5' LTR	WT	Non coding
	G->A	6223	Vpr	WT	Glu->Lys
SIVopt2	T->C	701	5' LTR	WT	Non coding
	T->C	829	5' LTR	WT	Non coding
	T->C	2613	Pol (PR)	WT	Val->Ala
	T->C	5806	Vif	WT	Val->Ala
	G->A	6238	Vpr	WT	Glu->Lys
	A->G	9287	Nef	WT	Arg->Gly

*Positions are numbered according to SIVMM239 sequence (http://www.hiv.lanl.gov).

Supplementary figure 1

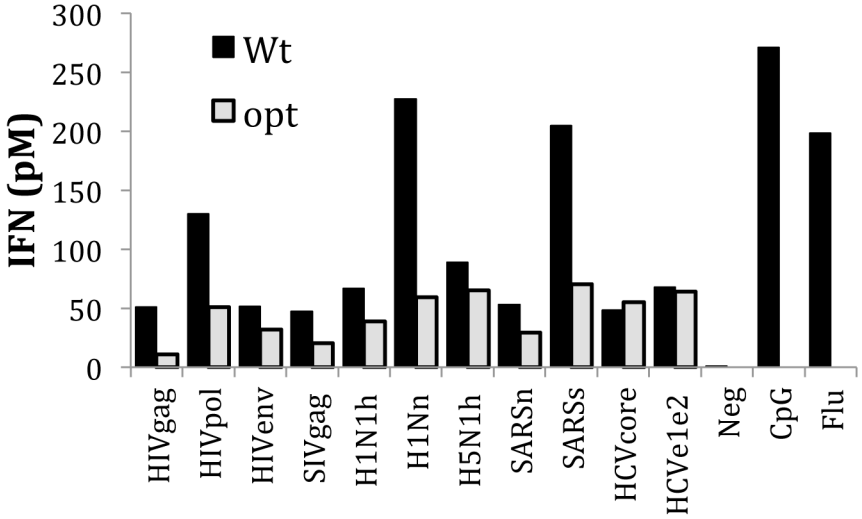
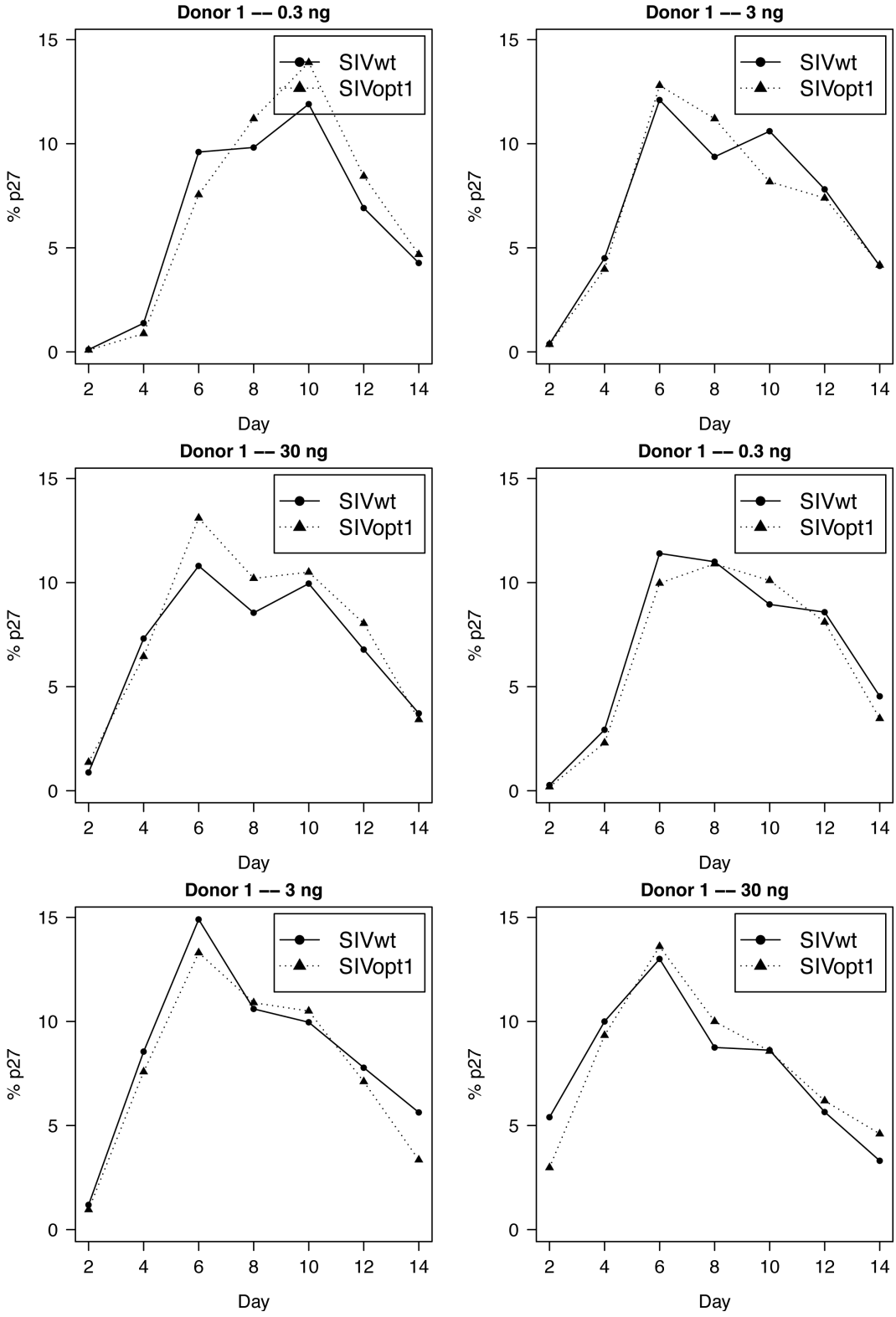


Figure S1. IFN-1 production by human PBMCs in response to wild type or humanized viral RNA. Human PBMC were stimulated by in vitro transcribed RNA complexed to DOTAP. Supernatant was collected 20h after transfection, and IFN-I produced was quantified using HL116 reporter cells. Neg: unstimulated PBMC), CpG oligonucleotides or influenza virus were used as positive controls.

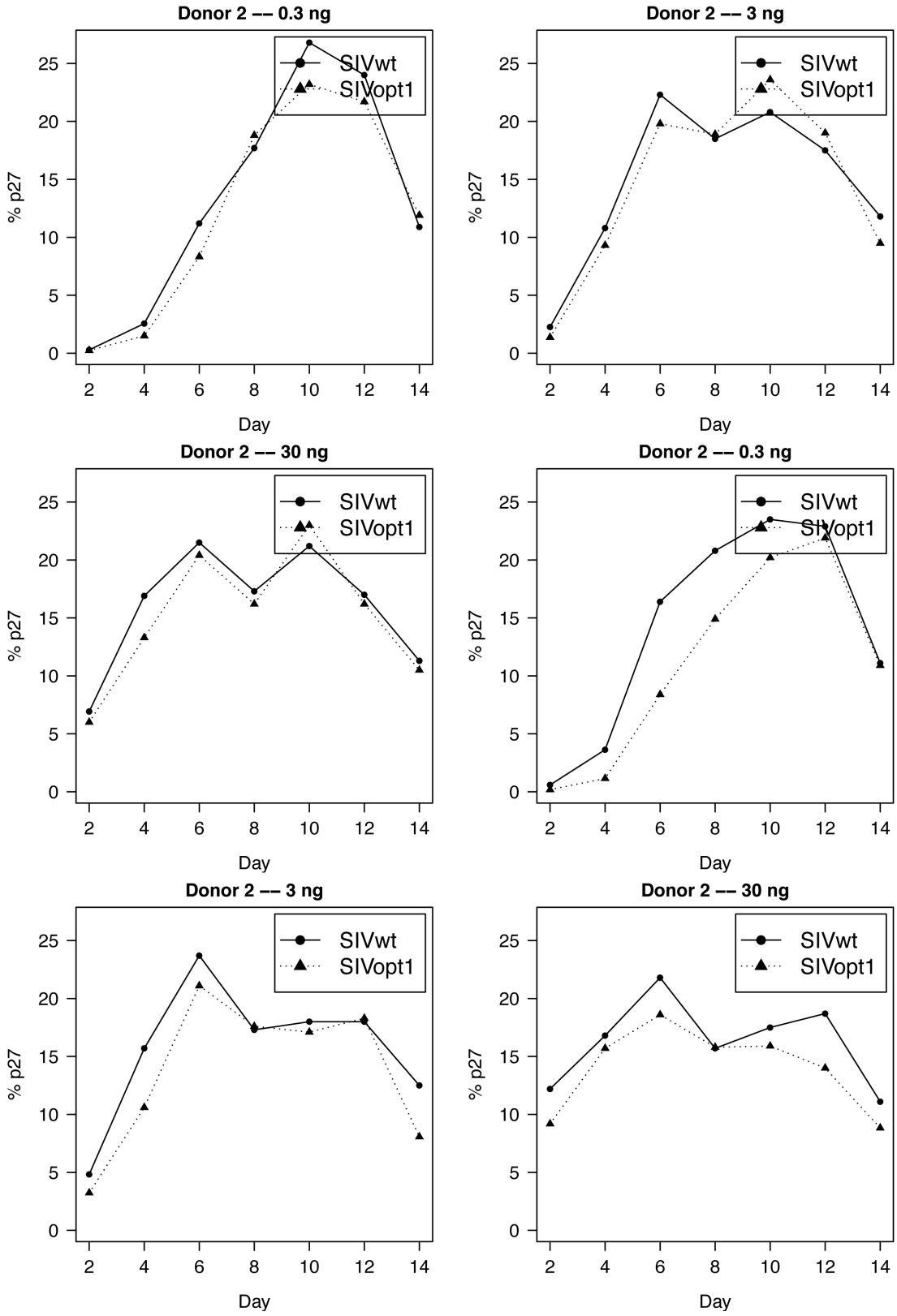
Stimulation of PBMC by in vitro transcribed RNA and interferon detection

Freshly extracted PBMC were separated from whole blood by Ficoll-Hypaque density gradient centrifugation and stimulated (10^6 cells /ml) with 2 µg/ml ssRNA complexed with N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium methylsulfate (DOTAP) (Roche). Unstimulated cells and cells treated only with DOTAP served as negative controls. After 20 h of stimulation, the level of IFN-I in supernatant was quantified using the reporter cell line HL116, that carries the luciferase gene under the control of IFN-inducible 6-16 promoter (41) (a kind gift from Sandra Pellegrini, Institut Pasteur, France).

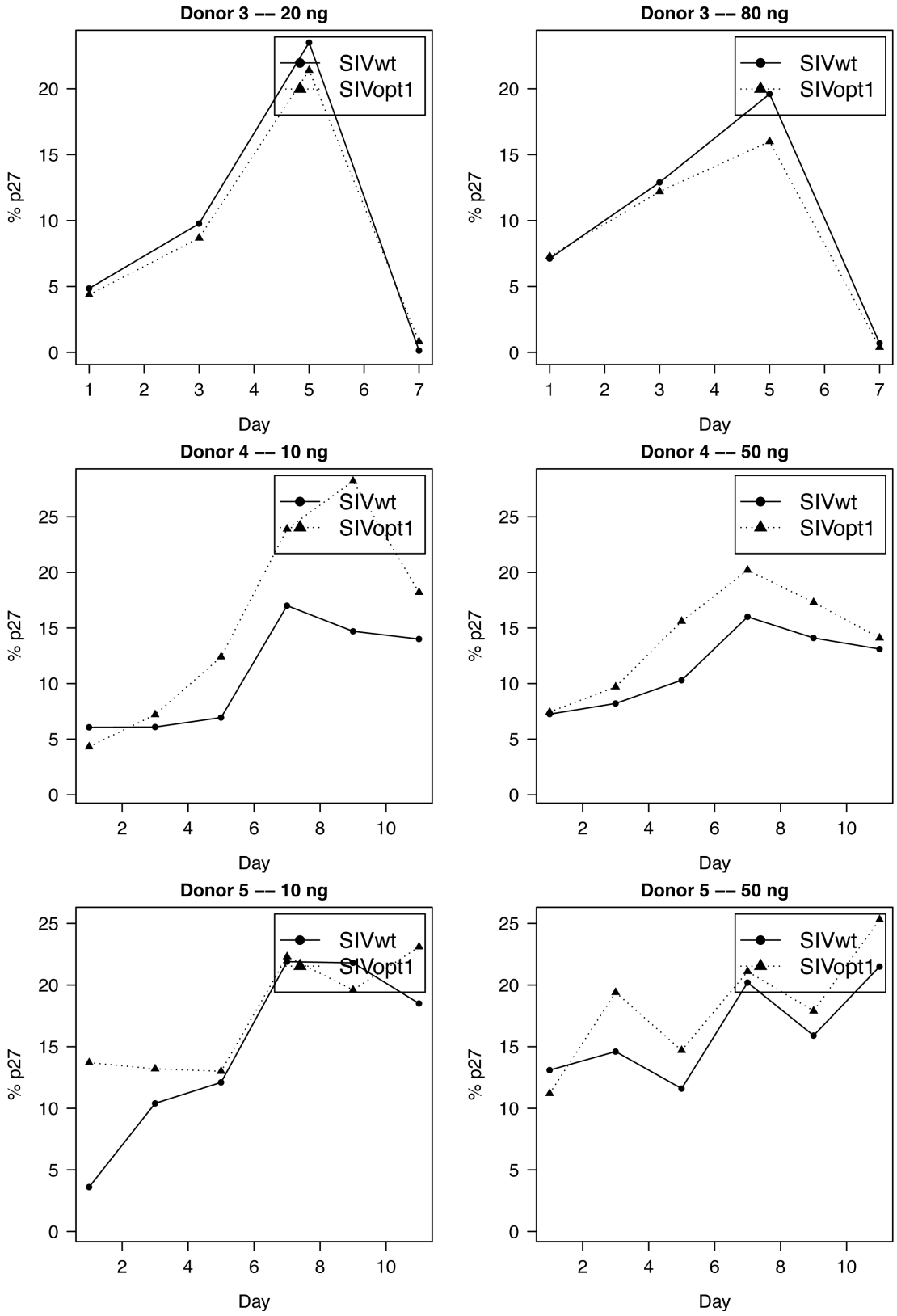
Supplementary figure 2-A



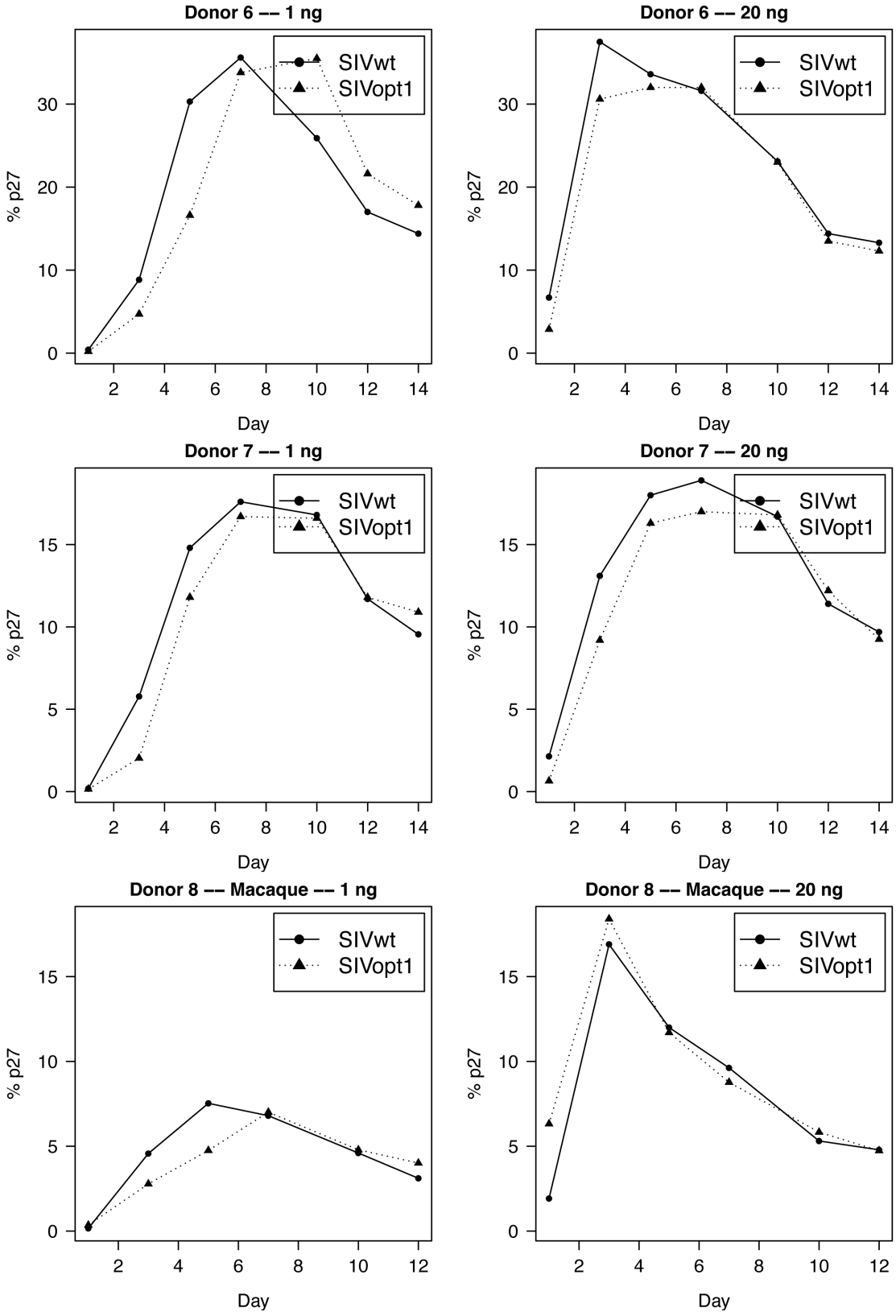
Supplementary figure 2-B



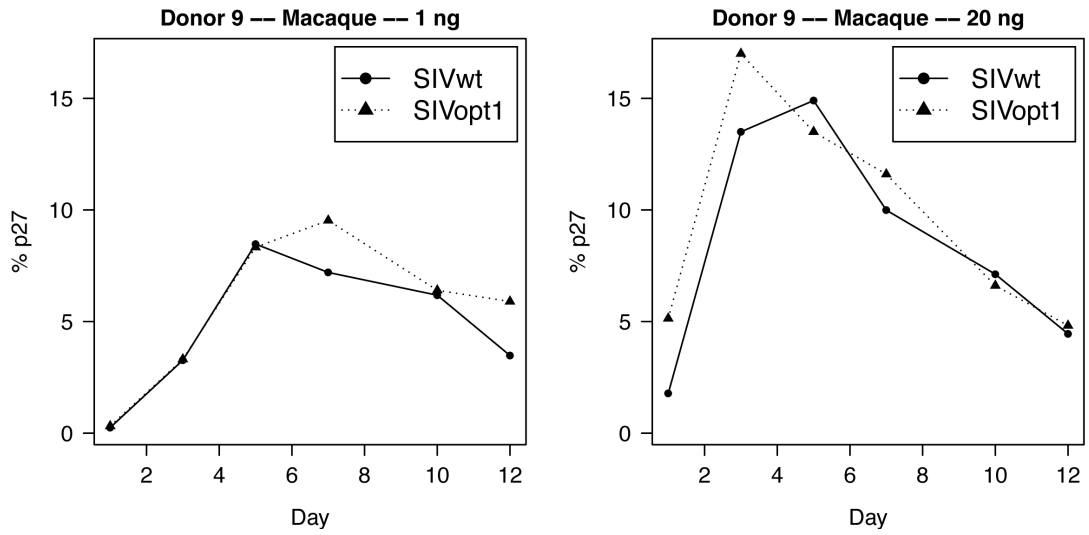
Supplementary figure 2-C



Supplementary figure 2-D

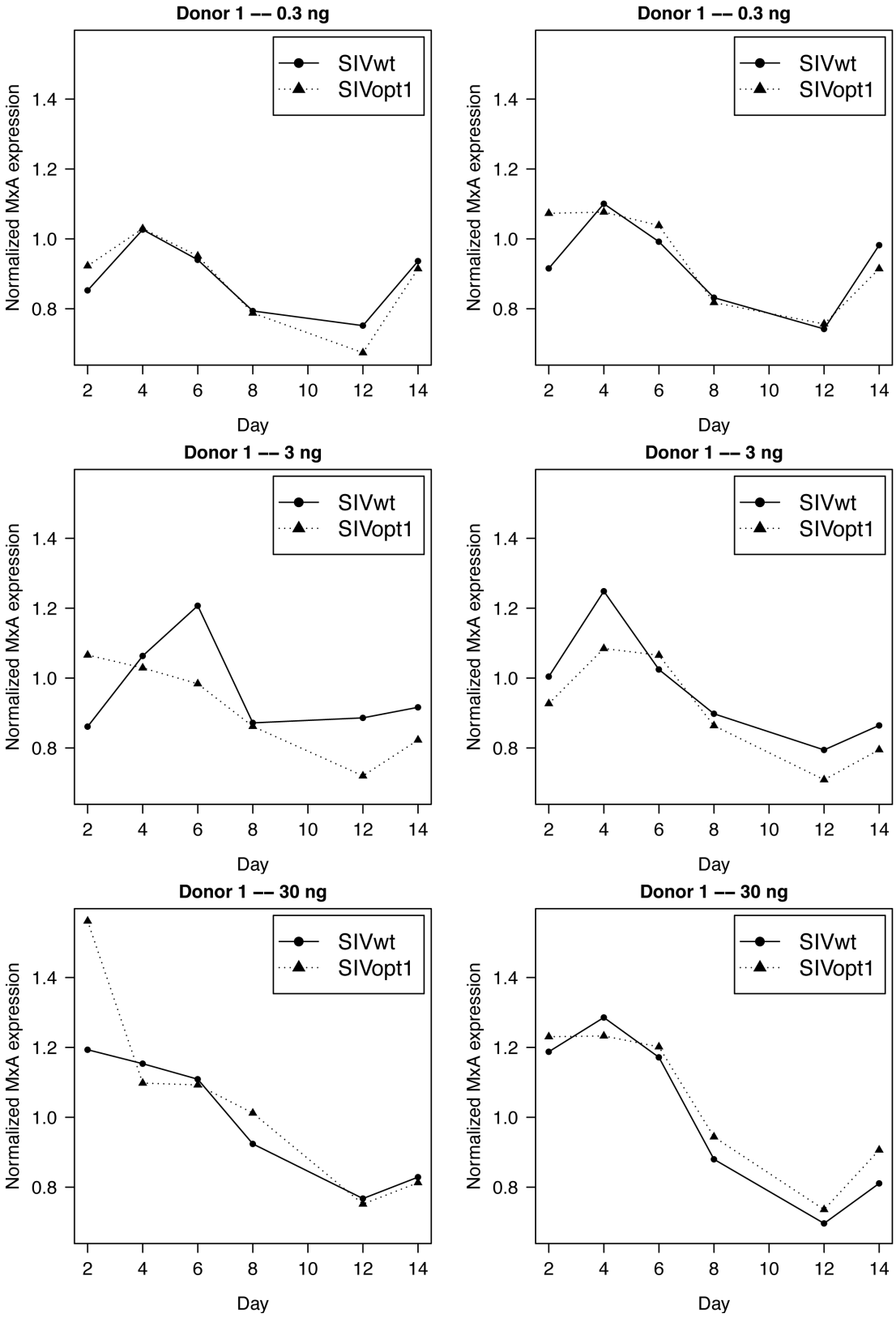


Supplementary figure 2-E

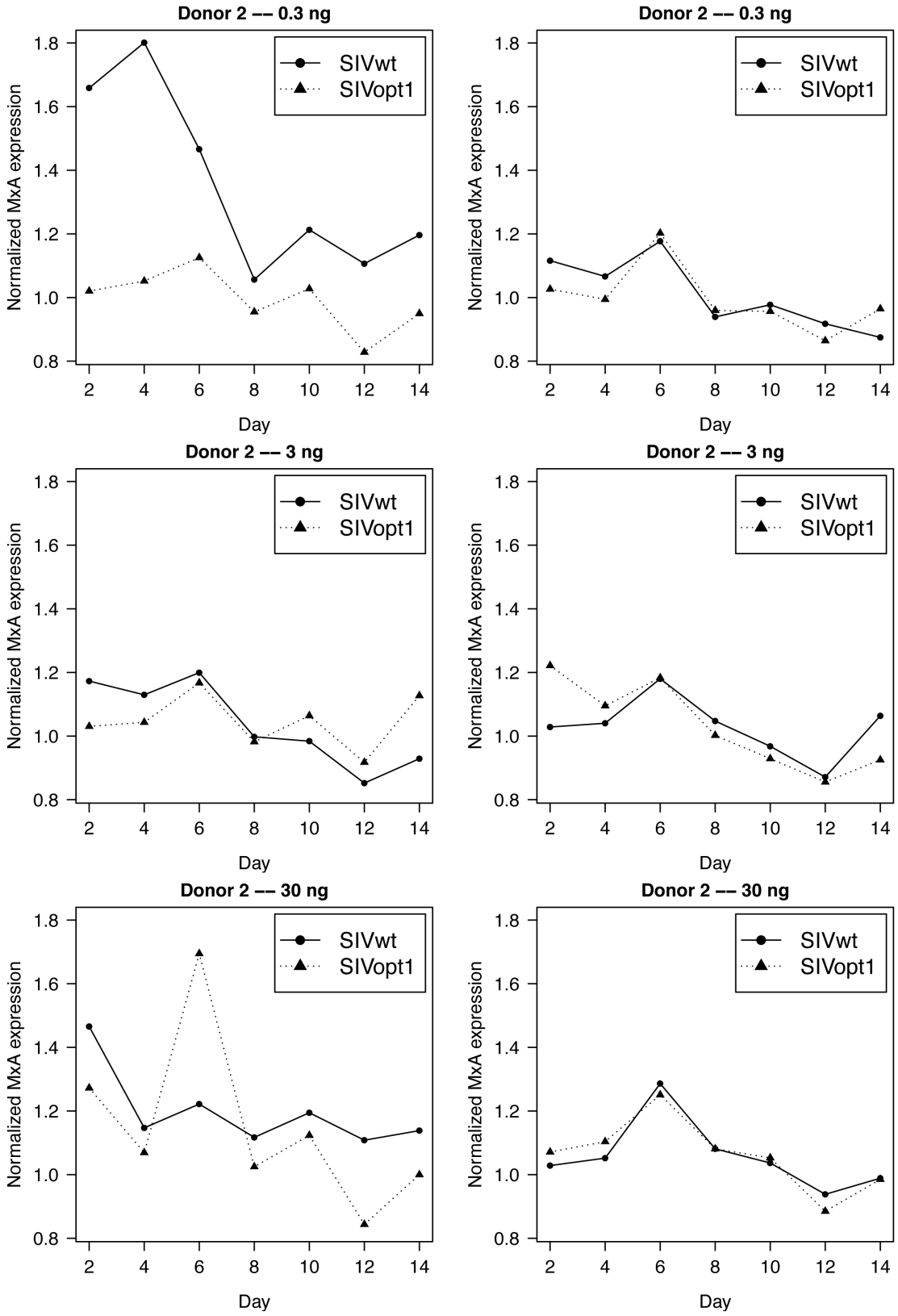


Supplementary figure S2 legend. Replicative capacity of SIVwt and SIVopt1 in PBMC. Human (donors 1 to 7) and macaque (donors 8 and 9) PBMC were infected by SIVwt or SIVopt1 (same data as in Fig. 4). The replicative kinetics are shown separately for each donor (two replicates have been done for donor 1 and 2). The amount of viral input used to infect cells is indicated (p27 ng).

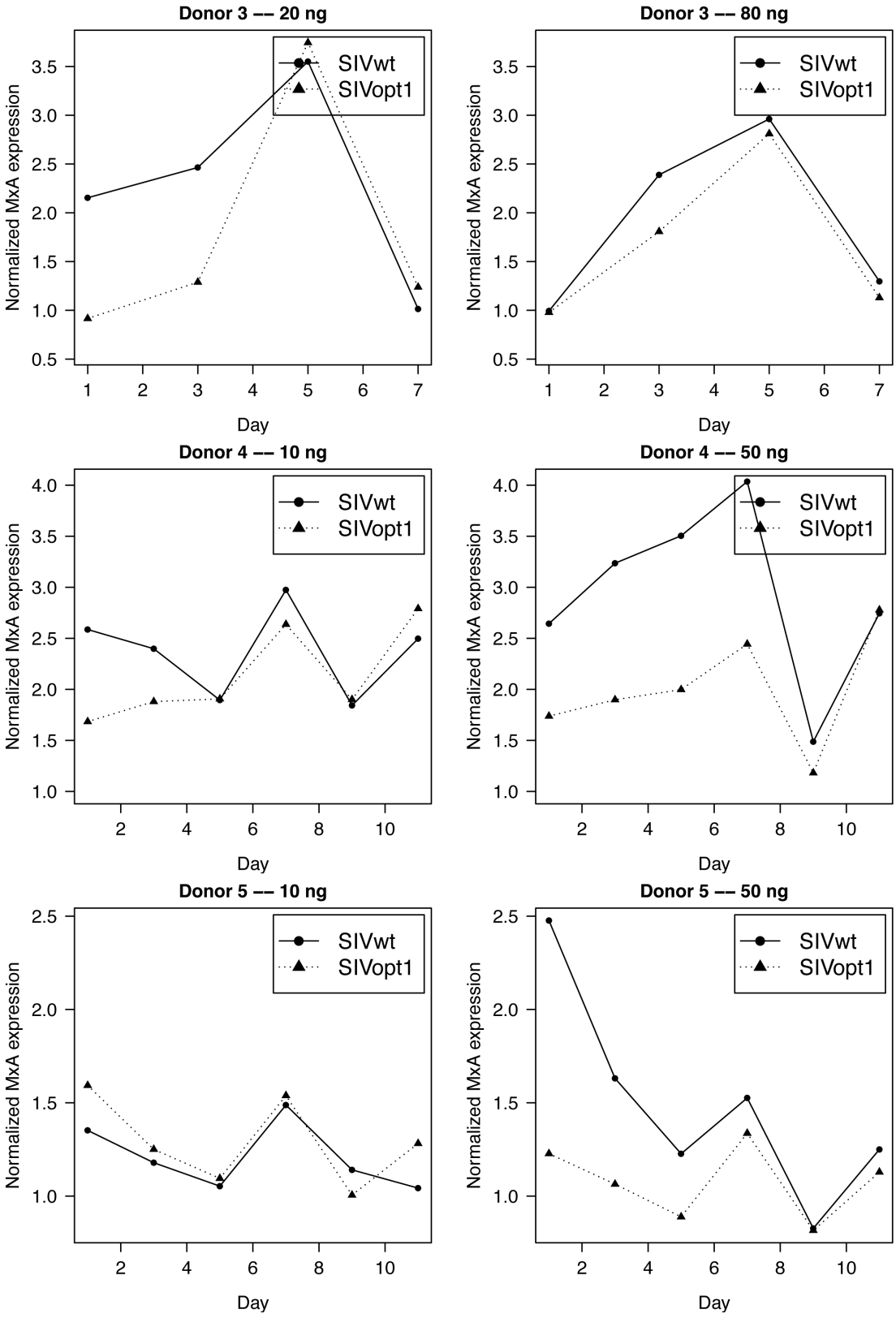
Supplementary figure 3-A



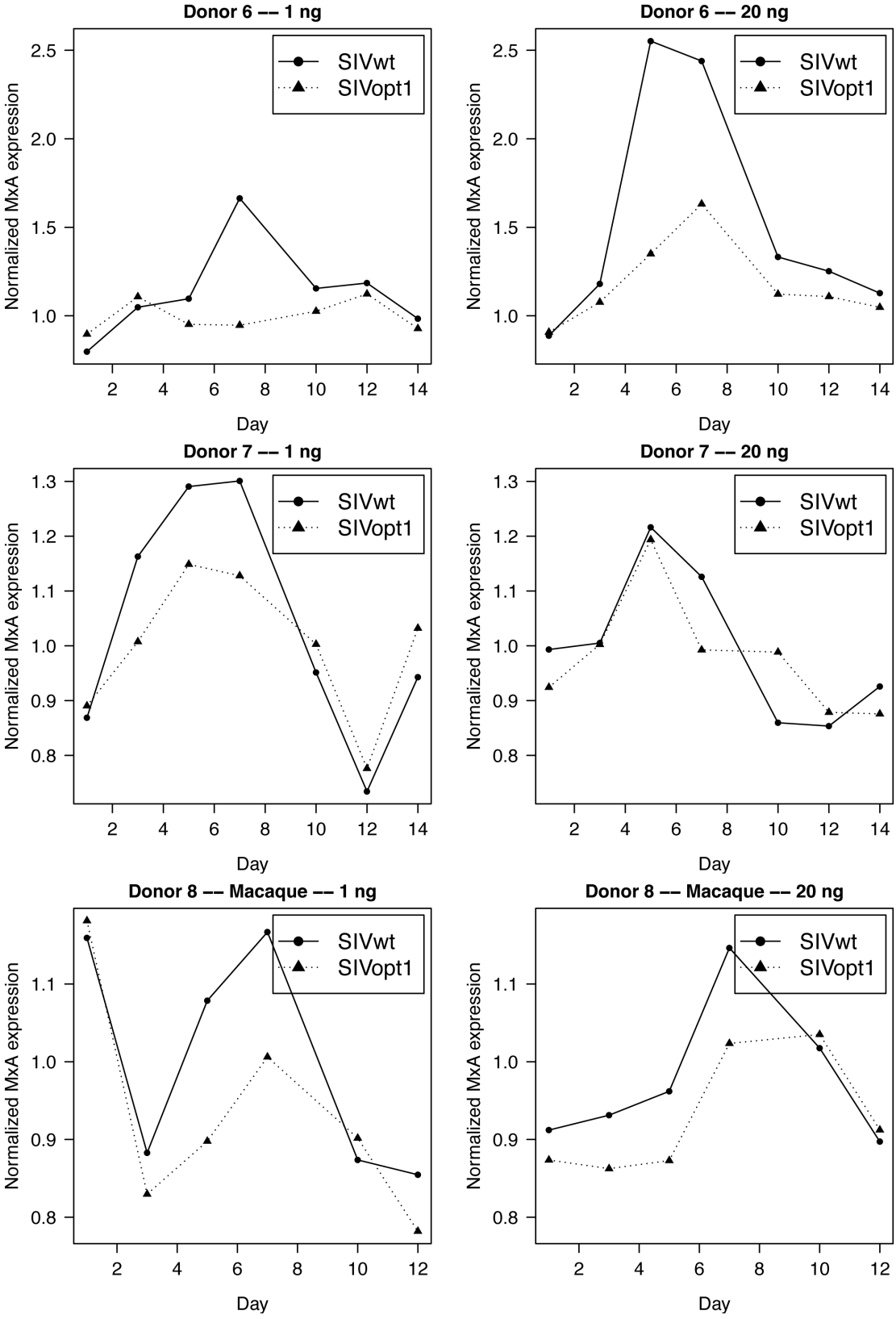
Supplementary figure 3-B



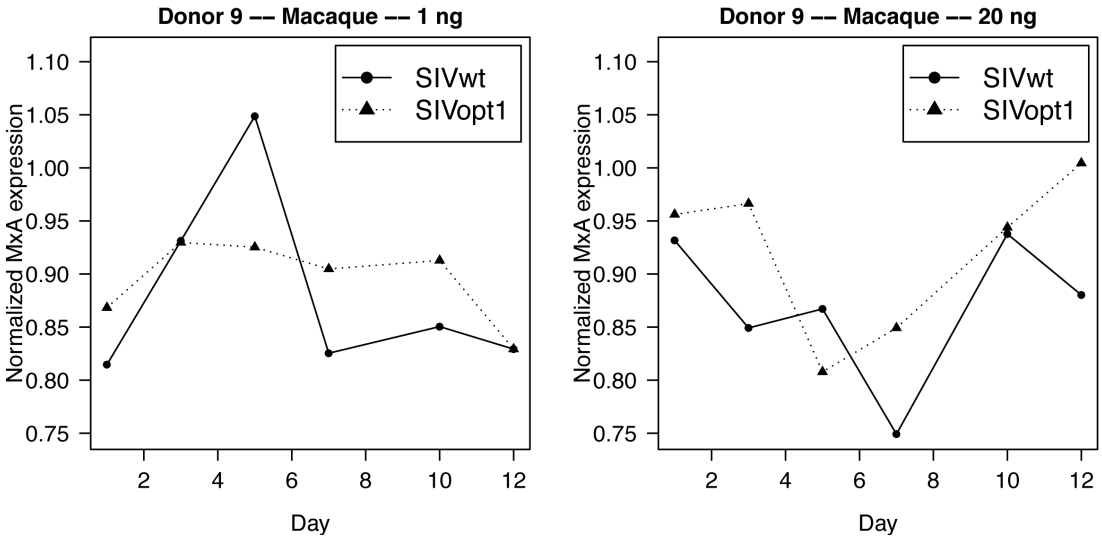
Supplementary figure 3-C



Supplementary figure 3-D



Supplementary figure 3-E



Supplementary figure S3 legend. Differential sensing of SIV replication in PBMC. Human (donors 1 to 7) and macaque (donors 8 and 9) PBMC were infected by SIVwt or SIVopt1 (same data as Fig. 4). IFN-I Induction was measured with the profile of intracellular MxA expression, an interferon stimulated gene. Data are shown separately for each donor (two replicates have been done for donor 1 and 2). The amount of viral input used to infect cells is indicated (p27 ng).