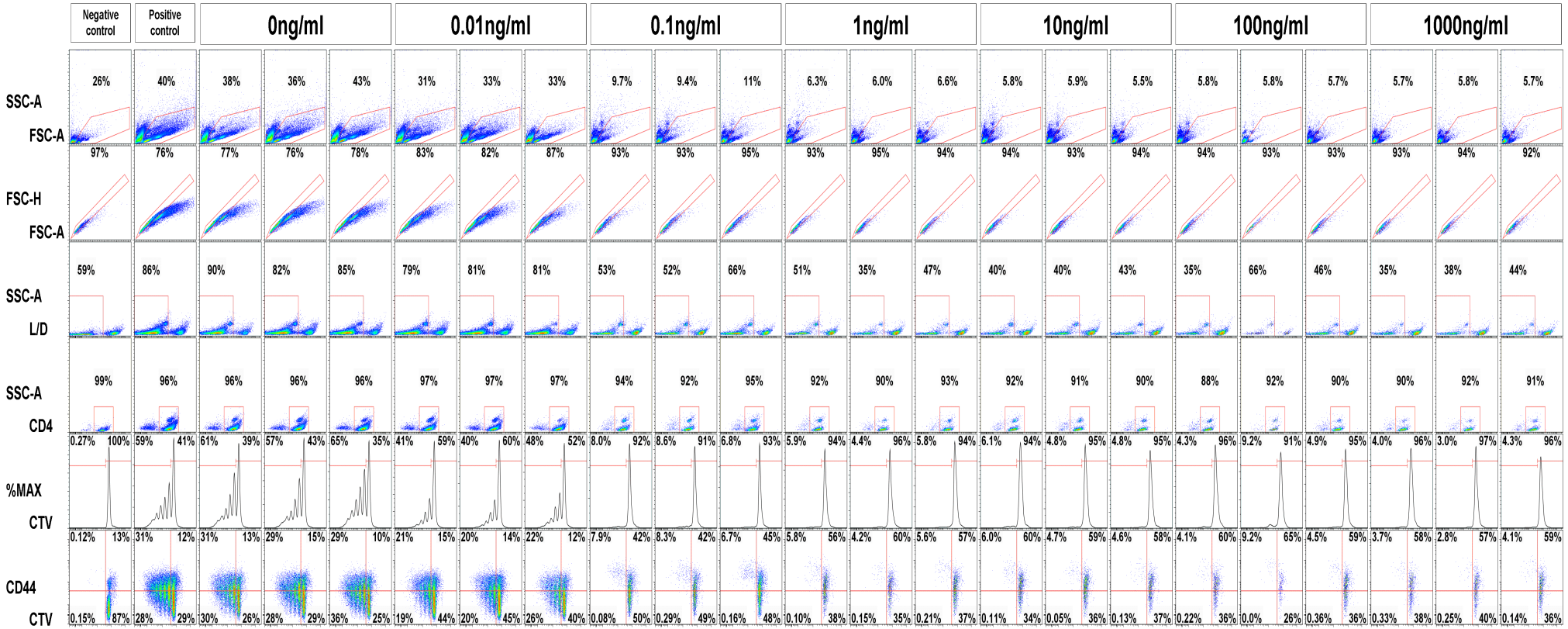
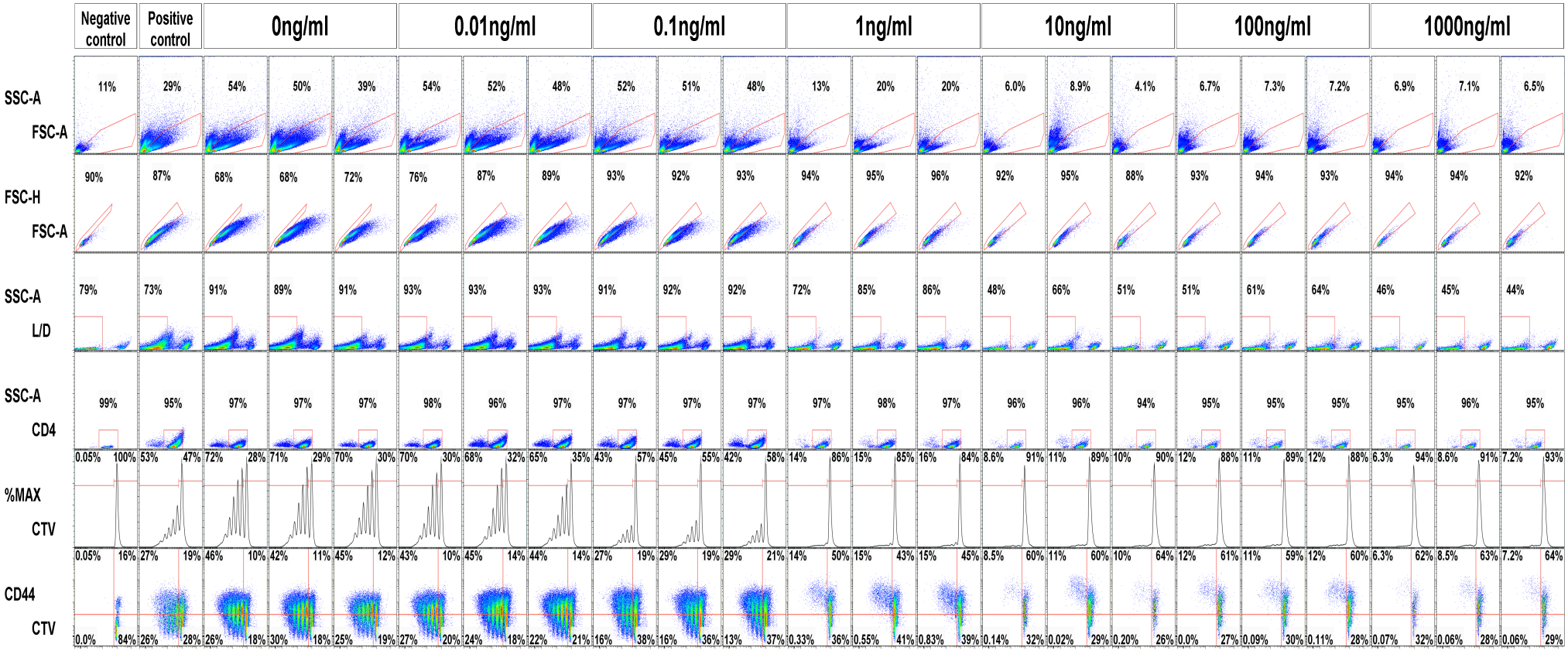
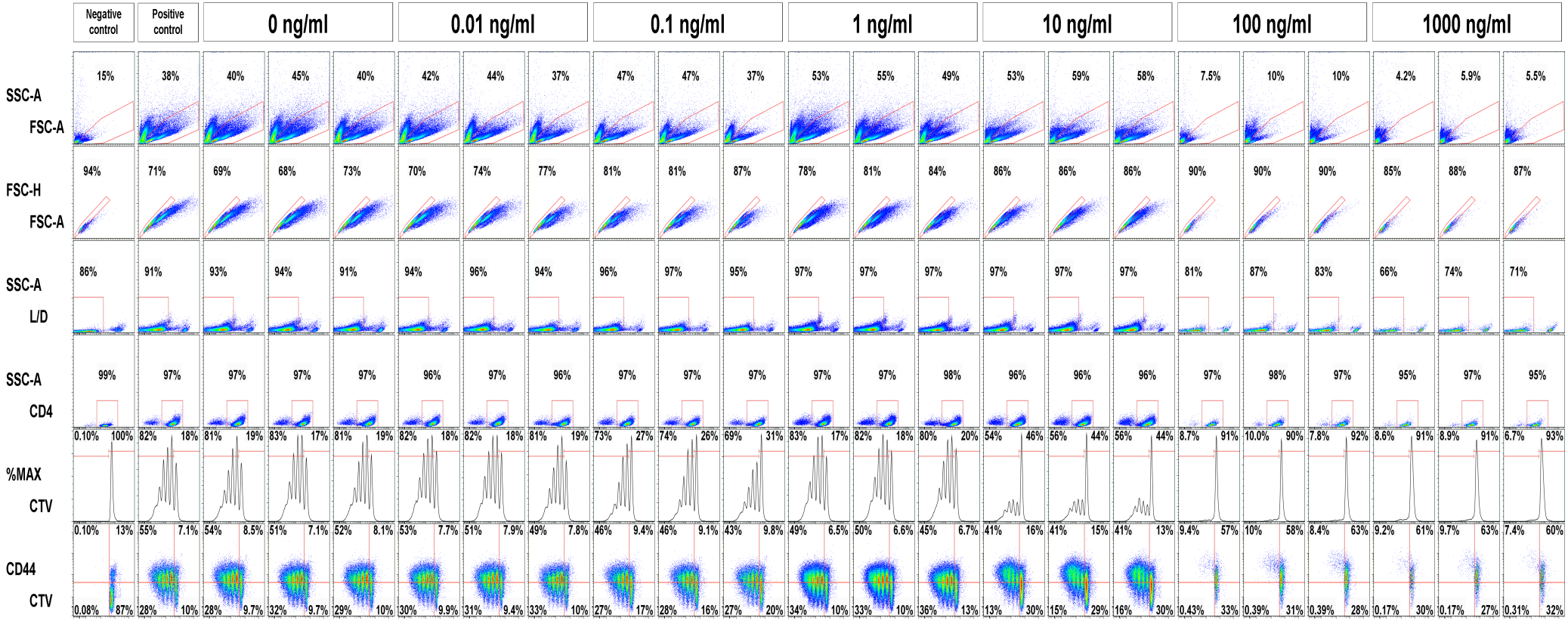
A. Raw data for FK506



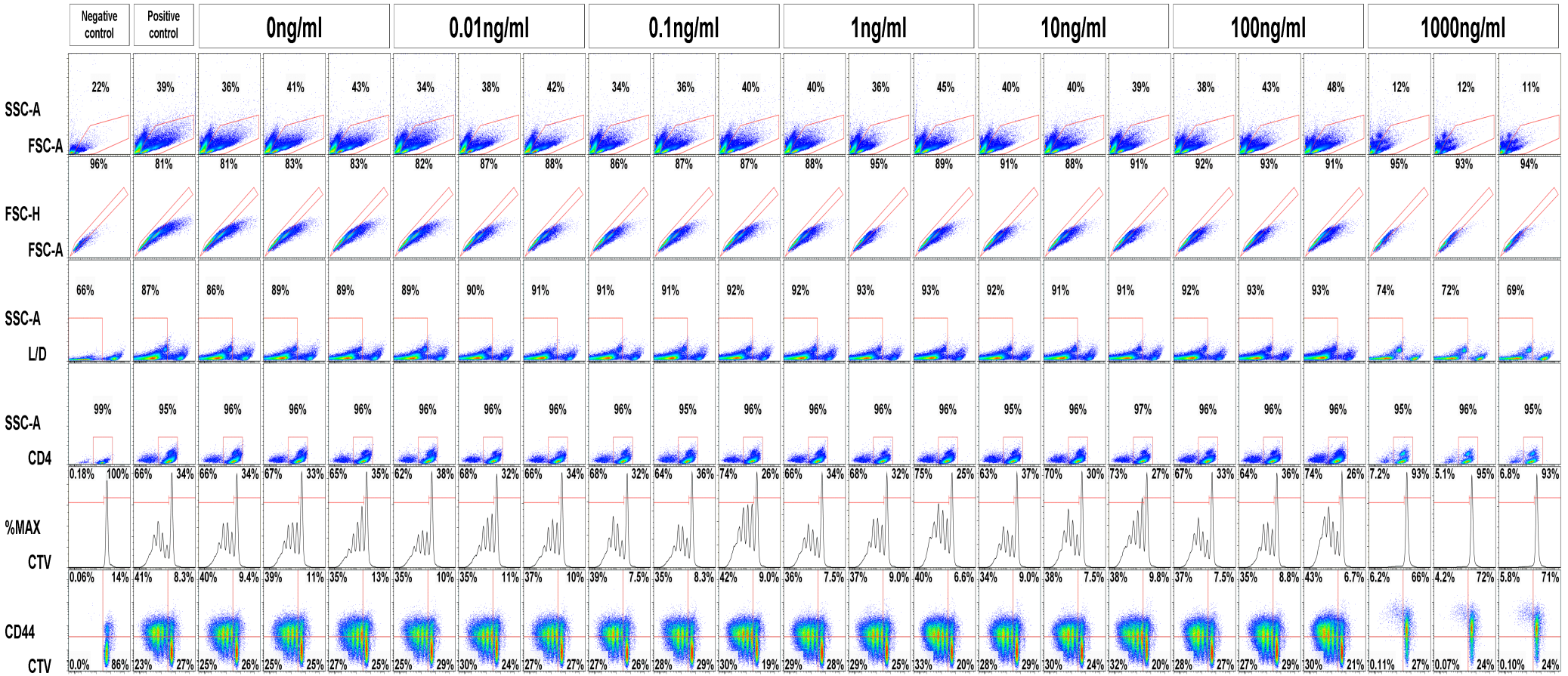
B. Raw data for 9-deoxo-FK506 (9D-FK506)



C. Raw data for 9-deoxo-31-*O*-demethyl-FK506 (9D31OD-FK506)



D. Raw data for 9-deoxo-prolyl-FK506 (9DP-FK506)



E. Raw data for 31-*O*-demethyl-FK506 (31OD-FK506)

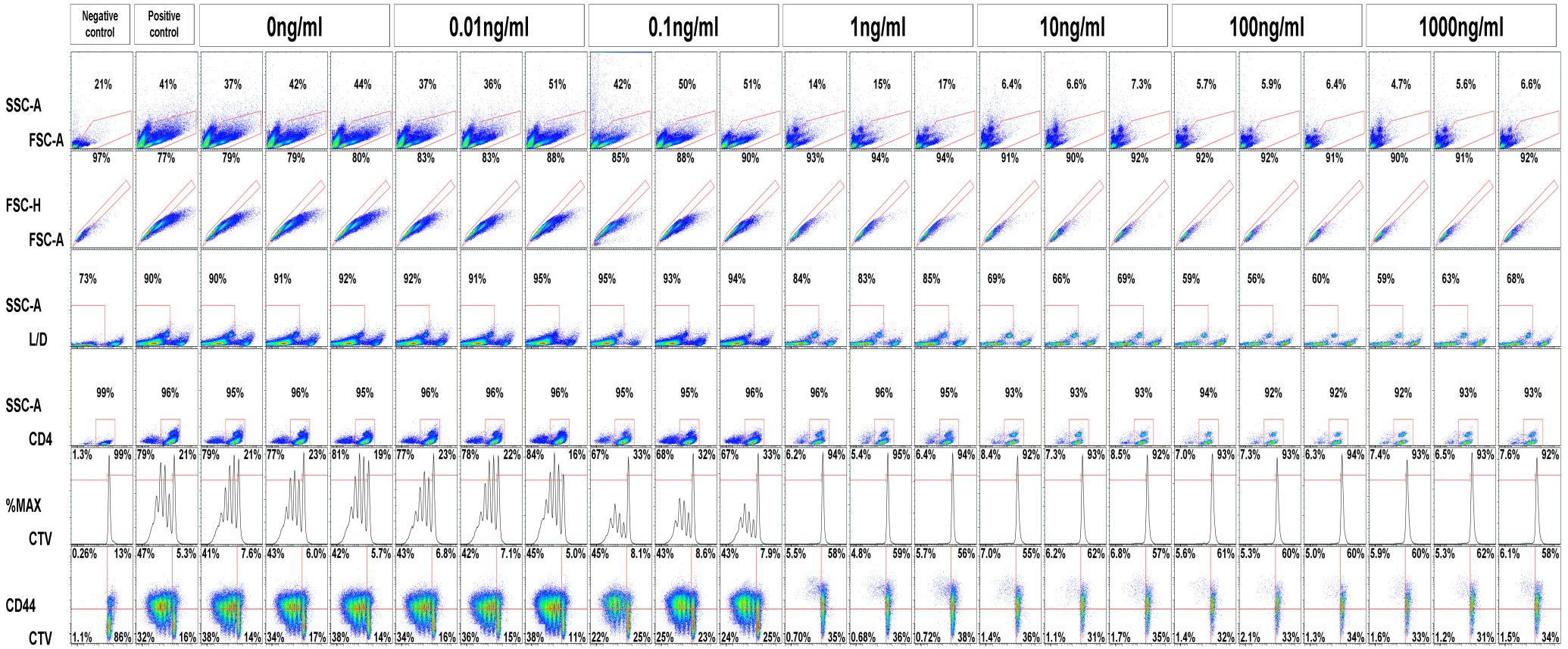


Figure S1. Raw data for the cytotoxicity and immunosuppressive effect of FK506 and FK506 analogs. The one representative set of raw FACS data for the cytotoxicity and immunosuppressive effect of FK506 (A), 9-deoxo-FK506 (9D-FK506) (B), 9-deoxo-31-*O*-demethyl-FK506 (9D31OD-FK506) (C), 9-deoxo-prolyl-FK506 (9DP-FK506) (D), and 31-*O*-demethyl-FK506 (31OD-FK506) (E) on the activated T-cells was shown. We repeated the experiments three times independently to get the cell cytotoxicity value and IC-50 curves shown in Figure 2B and 2D. Immunosuppressive effect of FK506 and the FK506 analogs on primary CD4+ T helper cells was assessed at various concentrations of FK506 and the FK506 analogs with three replicates using flow cytometry. (First row) Lymphocytes were selected within the boundaries from the forward scatter area (FSC-A) and side scatter area (SSC-A); (2nd row) single cells (within the red box) were selected from the forward scatter height (FSC-H) and forward scatter area (FSC-A) for further analysis; (3rd row) Primary cultured T cells from mice were stained with LIVE/DEAD™ cell viability kits and the percentage of live cells was determined in the presence of various concentrations of FK506; (4th row) $CD4^+$ helper T cells were isolated with CD4 T cell enrichment kits; (5th and 6th rows) Cell Trace™ Violet (CTV) was used to dye the cells immediately following culture, and intensity levels were measured to detect proliferation after 72 hours of drug exposure. The assay included a negative control group with inactivated T cells (NC), a positive control group with activated T cells (PC), and a vehicle group with activated T cells and a concentration of 0 μg/ml. The experiment performed with three replicates for each concentration of each FK506 analog compound tested across a range of concentrations. Multiple peaks indicating the proliferation of T cells diminished at concentrations associated with immune suppression. The percentage of proliferated cells within each group was normalized to that with the vehicle.

Table S1. *C. neoformans, C. albicans* and *A. fumigatus* strains used in this study

Strain	ATCC number	Species	Genotype	Reference
H99	208821	*C. neoformans*	*MAT*α	(1)
46.F.5.02	(Tanzania isolate)	*C. neoformans*		(2)
78.7.98	(Tanzania isolate)	*C. neoformans*		(2)
BT63	(Botswana isolate)	*C. neoformans*		(2)
BT130	(Botswana isolate)	*C. neoformans*		(2)
S25C	(Asia isolate)	*C. neoformans*		(2)
S25J	(Asia isolate)	*C. neoformans*		(2)
KCCM50544	2344	*C. neoformans*		(3)
KCCM50564	32045	*C. neoformans*		(4)
YSB64		*C. neoformans*	*MAT*α *hog1*Δ::*NAT*	(2)
YSB549		*C. neoformans*	*MAT*α *ire1*Δ::*NAT*	(5)
M049		*C. neoformans*	*ade2*Δ derivative of H99	(6)
MCC1		*C. neoformans*	*frr1*::*ADE2* of M049	(6)
KK1		*C. neoformans*	*MAT*α *cna1*Δ::*NAT*	(7)
KK2		*C. neoformans*	*MAT*α *cnb1*Δ::*NAT*	(7)
SC5314	MYA2876	*C. albicans*		(8)
12553	10259	*C. albicans*		(9)
12554	10261	*C. albicans*		(9)
11282	10231	*C. albicans*		(9)
50235	18804	*C. albicans*		(10)
50539	66422	*C. albicans*		This study
50582	24433	*C. albicans*		(11)
YAG171		*C. albicans*	*rbp1*Δ/*rbp1*Δ	(12)
YAG237		*C. albicans*	*CNB1-1*/*CNB1*	(12)
DAY364		*C. albicans*	*cnb1*Δ/*cnb1*Δ	(12)
Af293	MYA4609	*A. fumigatus*		(13)
KCCM32791	(Korean isolate)	*A. fumigatus*		This study

***Gray shaded strains were used for the MIC assay.**

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