

LIST OF FIGURES

1.1	Phylogeography of SIVcpz	3
1.2	HIV-1 genomic organization and virion structure	6
1.3	Retroviral life cycle	8
1.4	Ribbon representation of CypA and HIV-1 CA structure	10
1.5	Single cycle viral infectivity assay	14
2.1	HIV-1 infectivity is disrupted by CsA, the G89V and the P90A mutations in CA	17
2.2	Knockdown of CypA by RNAi reproduces the effect of CsA and G89V	20
2.3	Inhibition of HIV-1 infectivity by CsA is CA-dependent if drug is administered to target cells during virus entry but independent of the CA-CypA interaction if drug is present during virion production	22
2.4	Disruption of CypA incorporation into virions by competitive inhibitors of CypA-CA interaction	24
2.5	Melle ⁴ -CsA or Sangliffehrin inhibit infectious HIV-1 virion production independently of the CA-CypA interaction	26
2.6	Producer cell CypA has no effect on HIV-1 virion infectivity	28
2.7	Amino acid sequence alignment of the CypA binding regions from wild-type HIV-1 _{NL4-3} , the A92E mutant, the NL4-3/CA9 chimera, and the NL4-3/MVP5180 chimera	30
2.8	Cell-type specific effects of CsA on HIV-1 replication are determined by the target cell	31
2.9	Cell-specific phenotypes on HIV-1 replication are not determined by the producer cell	32
2.10	Target cell CypA regulates the cell-type specific effects on HIV-1 replication	34
2.11	CypA binding to HIV-1 CA is required for HeLa resistance to HIV-1 A92E	36

3.1	CsA disrupts Env incorporation into HIV-1 virions	38
3.2	Treatment of producer cells with CsA disrupts infectivity of gp160 pseudotyped HIV-1 virions in a dose-dependent manner	39
3.3	Envs from different lentiviruses are inhibited by CsA	40
3.4	CsA disrupts infectivity of HIV-1 virions pseudotyped with gp160, but not with VSV-G	41
3.5	CypB does not regulate gp160 processing	42
3.6	Cyp60 is not involved in processing of gp160	44
4.1	HIV-1, but not SIVmac is restricted in non-human primates	55
4.2	Restriction of retroviruses by primate TRIM5 α proteins	58
4.3	Graphic representation of primate TRIM5 α structure	59
5.1	Knockdown of endogenous TRIM5 α_{hu} enhances HIV-1 infectivity	64
5.2	Reduction of HIV-1 infectivity by CsA or CA mutant G89V is not mediated by TRIM5 α_{hu}	66
5.3	Reduction of HIV-1 infectivity by CypA knockdown is independent of TRIM5 α_{hu}	68
5.4	Reduction of HIV-1 infectivity by CsA or G89V mutation is independent on TRIM5 α_{hu} in human T-cell lines	70
5.5	Promotion of HIV-1 infectivity by CypA is independent of TRIM5 α_{hu} regardless of the route of viral entry	72
5.6	Promotion of HIV-1 infectivity by CypA is independent of TRIM5 α_{hu} regardless of the route of viral entry	73
5.7	HIV-1 VLPs ability to abrogate N-MLV restriction in TE671 cells is enhanced if CypA expression is knocked down	75
5.8	TRIM5 α knockdown eliminates the stimulatory effect of As ₂ O ₃ in TE671 cells	77
6.1	Restriction of the CA mutant A92E can not be overcome by As ₂ O ₃	79

6.2	CsA-dependence of HIV-1 CA mutant A92E is TRIM5 α_{hu} -independent	80
6.3	CypA expression levels among different cell types	82
6.4	Restriction to A92E is not saturable by VLPs	83
6.5	Restriction of A92E is not saturable by TRIM5 α -susceptible CAs	84
7.1	Proposed model for restriction of N-MLV and HIV-1	88