SIV replication in human cells

Ryuta Sakuma and Hiroaki Takeuchi*
Department of Molecular Virology, Tokyo Medical and Dental University, Tokyo, Japan

Current human immunodeficiency virus type 1 pandemic is believed to originate from cross-species transmission of simian immunodeficiency virus (SIV) into human population. Such cross-species transmission, however, is not efficient in general, because viral replication is modulated by host cell factors, with the species-specificity of these factors affecting viral tropism. An understanding of those host cell factors that affect viral replication contributes to elucidation of the mechanism for determination of viral tropism. This review will focus on an anti-viral effect of ApoB mRNA editing catalytic subunit, tripartite motif protein 5 alpha, and cyclophilins on SIV replication and provide insight into the mechanism of species-specific barriers against viral infection in human cells. It will then present our current understanding of the mechanism that may explain zoonotic transmission of retroviruses.

Keywords: HIV-1, SIV, APOBEC3G, TRIM5α, cyclophilin A, cyclophilin B

INTRODUCTION

There is significant evidence that the ongoing worldwide acquired immunodeficiency syndrome (AIDS) epidemic was caused by cross-species transmission of simian immunodeficiency viruses (SIVs) into the human population. Replication of primate lentiviruses in their natural hosts is generally non-pathogenic; however, cross-species transmission of these viruses can result in highly pathogenic phenotypes. How and when this transmission occurred is still debated but it is now generally accepted that HIV-2 originated from a sooty mangabey strain of SIV (SIVsm; Gautsch et al., 1978; Towers et al., 2000) and HIV-1 appears to have originated from a chimpanzee strain of SIV (SIVcpz; Gao et al., 1999). Zoonotic transmission of SIVs, however, is not common and is controlled by host factors that generally prohibit SIV replication in human hosts and many human-derived cell lines.

Viral replication is modulated by host cell factors, with the species-specificity of these factors affecting viral tropism. Some of these host factors can restrict viral replication and the anti-viral systems mediated by such host restriction factors, termed intrinsic immunity, play an important role in determining species-specific barriers against viral infection. For instance, Fv-1 in mice is known to restrict replication of a murine leukemia virus (Rein et al., 1976; Towers et al., 2000) and tripartite interaction motif 5α (TRIM5α) recently has been found to be responsible for restricting HIV-1 but not SIV infection in Old World monkey (OWM) cells (Hatziioannou et al., 2004b; Keckesova et al., 2004; Stremlau et al., 2004; Yap et al., 2004; Song et al., 2005; Yinon et al., 2005). Restriction of retroviral replication by these host cell factors takes place after viral entry, but before the integration step, and the viral determinants for this type of restriction have been mapped to the capsid (CA) protein (Gautsch et al., 1978; Korak and Chakraborti, 1990; Towers et al., 2000; Goff, 2004; Stremlau et al., 2006). Two recent studies showed that the cellular protein SAMHD1 is myeloid-lineage cell-specific HIV-1 restriction factor counteracted by Vpx proteins from HIV-2 and SIVm (Hireka et al., 2011; Laguette et al., 2011). Restriction of lentivirus infection by SAMHD1 is likely to take place at the reverse transcription step. Another anti-retroviral protein, tetherin (also referred to as BST-2, CD317, or HML-1) inhibits retrovirus release and is antagonized by HIV-1 Vpu protein, Nef protein of many SIVs, or Env protein of HIV-2 (Neil et al., 2008; Le Tortorec and Neil, 2009; Zhang et al., 2009). Understanding how host cell factors affect viral replication, positively or negatively, would contribute to elucidating the molecular mechanism that determines viral tropism. Here, we discuss an anti-viral effect of ApoB mRNA editing catalytic subunit (APOBEC), TRIM5α, and cyclophilins (Cyps) on SIV replication.

APOBEC: ENZYMATIC RESTRICTION FACTOR THAT TARGETS RETROVIRUSES

Replication of HIV-1 in primary CD4+ T cells, monocyte, and some immortalized T cell lines depends on the presence of the HIV-1 accessory gene product, Vif (standing for virus infectivity factor; Fisher et al., 1987; Strebel et al., 1987), and it works in a host cell-specific manner. Vif is required for enhanced HIV-1 replication in some cell types called non-permissive cells. In contrast, HIV-1 replication is Vif-independent in permissive cells (Akari et al., 1992; Fan and Peden, 1992; Gabasda et al., 1993; Blanc et al., 1993; Sakai et al., 1993; von Schwedler et al., 1993; Borman et al., 1993). Recently, some cytidine deaminases were identified as a new class of host restriction factors that target retroviruses such as HIV-1 or SIV (Harris and Liddard, 2004; Cullen, 2006). APOBEC3G (Apo3G), a member of the APOBEC family of cytidine deaminases, is the first identified enzymatic restriction factor and the determinant that makes cells permissive or non-permissive. Apo3G is also a host factor that restricts replication of human and simian lentiviruses in their respective target cells. Unlike TRIM5α or Fv-1, Apo3G does not exert its anti-viral activity by targeting the viral CA protein, but it is to be incorporated
Vif expression. During the production of progeny virions, Vif inhibits HIV-1 infection in the absence of Vif (Bishop et al., 2004a; another member of the family, APOBEC3F (Apo3F) was shown to potent anti-HIV-1 activity among the APOBEC family of proteins, demonstrated that SIVagm Vif supported replication of SIVagm for example, a report from the laboratory of Klaus Strebel et al., 2004).

APOBEC family members function to neutralize specific species-specific (Simon et al., 1998; Mariani et al., 2003). Accord-

ingly, hApo3G is insensitive to SIVagm Vif while African green monkey Apo3G (agmApo3G) is insensitive to HIV-1 Vif and the corresponding domain of TRIM5α. Its RING domain has E3 ubiquitin ligase activity. It self-ubiquitination occurs TRIM5α is quickly degraded (Diaz-Griffino et al., 2006). This rapid degradation of TRIM5α is not required for post-entry restriction since replacement of TRIM5α RING domain with the corresponding domain of TRIM21, which has lower self-ubiquitination activity and a longer half-life than TRIM5α does not alter the anti-viral activity (Kae et al., 2008). Recently, the laboratory of Dr. Mark Yeager discussed a novel architecture made with dimers of TRIM5α-21R. TRIM5α-21R forms a dimer through its B-box 2 and coiled-coil domains, and these dimers form six-sided rings on CA lattices to promote rapid core disassembly. Overexpression of TRIM5α leads to the formation of cytoplasmic bodies and is believed to be required for its anti-viral activity (Ike et al., 2008). During TRIM5α-mediated post-entry restriction, disassembly of viral cores is induced too quickly and the accumu-
late viral products is reduced (Stremlau et al., 2006). On the other hand, MG132 treatment inhibited quick-disassembly, yet HIV-1 infectivity was still restricted. Two reports showed that TRIM5α could block not only viral cDNA accumulation but also the nuclear import of viral cDNA (Berthoux et al., 2004; Wu et al., 2006). Thus, TRIM5α-mediated post-entry restriction is thought to have at least two phases: (i) TRIM5α induces rapid disassembly of viral core in a proteasome-dependent manner and (ii) TRIM5α degrades HIV-1 cDNAs in a proteasome-independent manner. The determinant of specificity and magnitude of the post-entry

into a newly synthesized virion during a production step, and then inhibits virus replication by targeting single-stranded viral cDNA during a subsequent infection step. HIV-1 counteracts Apo3G with Vif expression. During the production of progeny virions, Vif binds to Apo3G and induces Apo3G's proteasomal degradation, resulting in the decreased steady-state levels of human Apo3G (hApo3G; Yu et al., 2003).

There are anti-retroviral mechanisms of Apo3G against HIV-1 infection. First, Apo3G-containing virus can accumulate in a large number of substitutions that register as cytidine (C) to deoxyuridine (dU) in a virus minus-strand during reverse transcription, resulting guanine (G) to adenine (A) mutations in a viral plus-strand, known as “G-to-A hypermutation” (Harris et al., 2003; Lecossier et al., 2003; Mangeat et al., 2003; Mariani et al., 2003; Zhang et al., 2003; Yu et al., 2004b). Second, Apo3G can inhibit rRNA annealing or rRNA processing during reverse transcription (Guo et al., 2006; 2007; Mfisa et al., 2007). Third, Apo3G inhibits DNA strand transfer or integration (Li et al., 2007; Luo et al., 2008). Apo3G can inhibit virus replication by targeting single-stranded viral cDNA into a newly synthesized virion during a production step, and then inhibits viral plus-strand, known as “G-to-A hypermutation” (Harris et al., 2003; Lecossier et al., 2003; Mangeat et al., 2003; Mariani et al., 2003; Zhang et al., 2003; Yu et al., 2004b). TRIM5α captures HIV-1 core at a very early step(s) after infection, immediately after the release of the core into cytoplas.

To restrict HIV-1 infection and to recognize viral core, TRIM5α must oligomerize through its B-box 2 and coiled-coil domains (Mische et al., 2005; Li and Sodroski, 2008). Its RING domain has E3 ubiquitin ligase activity. It self-ubiquitination occurs TRIM5α is quickly degraded (Diaz-Griffino et al., 2006).

Thus, the presence and absence of Vif (Bishop et al., 2004a; Doehle et al., 2004; Liddament et al., 2004; Wiegand et al., 2004; Zheng et al., 2004), whereas APOBEC3B (Apo3B) can inhibit HIV-1 infection in both TRIM5α-mediated post-entry restriction, disassembly of viral cores is induced too quickly and the accumu-

lation of viral RT-products is reduced (Stremlau et al., 2006). On the other hand, MG132 treatment inhibited quick-disassembly, yet HIV-1 infectivity was still restricted. Two reports showed that TRIM5α degrades HIV-1 cDNAs in a proteasome-independent manner. The determinant of specificity and magnitude of the post-entry

The host protein which dictates Ref1 activity was identified as an α-isofrom of rhesus macaque TRIM5 protein by the laboratory of Dr. Joseph Sodroski (Stremelau et al., 2004). TRIM5 is a member of the TRIM family of proteins, and has RING, B-box 2, and coiled-coil as common and conserved domains among the family and B30.2 (PRYSPRY) domain on its C-terminal region (Nisole et al., 2005). Subsequently, the human and non-human primate homologs of TRIM5α were shown to restrict retroviruses, such as N-MLV, and equine infectious anemia virus (Hatziissiamou et al., 2004b; Keckesova et al., 2004; Perron et al., 2004; Yip et al., 2004; Song et al., 2005; Ylenen et al., 2005; Si et al., 2006). Rhesus monkey TRIM5α (nTRIM5α) has strong anti-HIV-1 activity but only modestly restricts SIV isolated from a macaque monkey (SIVmac) and does not block MLV infection, whereas its human homolog does not restrict HIV-1 infection.

TRIM5α recognizes incoming viral cores, but not a nononcogenic CA protein, thorough its B30.2 (PRYSPRY) domain. B-box 2 and coiled-coil domains are required for TRIM5α multimerization, and both coiled-coil and B30.2 (PRYSPRY) domains are essential for viral core binding (Reymond et al., 2001; Stermlau et al., 2006). TRIM5α captures HIV-1 core at a very early step(s) after infection, immediately after the release of the core into cyto-

T. the determinants of specific and magnitude of the post-entry

References

Morita et al., 2009). During TRIM5α-mediated post-entry restriction, disassembly of viral cores is induced too quickly and the accumu-
lation of viral RT-products is reduced (Stermlau et al., 2006). On the other hand, MG132 treatment inhibited quick-disassembly, yet HIV-1 infectivity was still restricted. Two reports showed that TRIM5α could block not only viral cDNA accumulation but also the nuclear import of viral cDNA (Berthoux et al., 2004; Wu et al., 2006). Thus, TRIM5α-mediated post-entry restriction is thought to have at least two phases: (i) TRIM5α induces rapid disassembly of viral core in a proteasome-dependent manner and (ii) TRIM5α degrades HIV-1 cDNAs in a proteasome-independent manner. The determinant of specificity and magnitude of the post-entry

References

Morita et al., 2009). During TRIM5α-mediated post-entry restriction, disassembly of viral cores is induced too quickly and the accumu-
lation of viral RT-products is reduced (Stermlau et al., 2006). On the other hand, MG132 treatment inhibited quick-disassembly, yet HIV-1 infectivity was still restricted. Two reports showed that TRIM5α could block not only viral cDNA accumulation but also the nuclear import of viral cDNA (Berthoux et al., 2004; Wu et al., 2006). Thus, TRIM5α-mediated post-entry restriction is thought to have at least two phases: (i) TRIM5α induces rapid disassembly of viral core in a proteasome-dependent manner and (ii) TRIM5α degrades HIV-1 cDNAs in a proteasome-independent manner. The determinant of specificity and magnitude of the post-entry

References

Morita et al., 2009). During TRIM5α-mediated post-entry restriction, disassembly of viral cores is induced too quickly and the accumu-
lation of viral RT-products is reduced (Stermlau et al., 2006). On the other hand, MG132 treatment inhibited quick-disassembly, yet HIV-1 infectivity was still restricted. Two reports showed that TRIM5α could block not only viral cDNA accumulation but also the nuclear import of viral cDNA (Berthoux et al., 2004; Wu et al., 2006). Thus, TRIM5α-mediated post-entry restriction is thought to have at least two phases: (i) TRIM5α induces rapid disassembly of viral core in a proteasome-dependent manner and (ii) TRIM5α degrades HIV-1 cDNAs in a proteasome-independent manner. The determinant of specificity and magnitude of the post-entry
Although TRIM5α et al., 1989). The binding of CsA to CypA inhibits this isomerase activity (Takahashi et al., 1989). In retrovirus replication, CypA was found to bind HIV-1 CA in the yeast two-hybrid system (Luban et al., 1993). The sequence Ala89-Gly89-Pro90-Ile91 of CA protein is the major fragment bound to the active site of CypA (Franke et al., 1994; Gamble et al., 1996; Zhao et al., 1997). Interestingly, The peptideyl-prolyl bond between Gly89 and Pro90 of the CA fragment has a trans conformation, in contrast to the cis conformation observed in other known CypA–peptide complexes (Zhao et al., 1997; Bosco et al., 2002), and Gly89 preceding Pro90 has an unfavorable backbone formation usually only adopted by glycine, suggesting that special Gly89-Pro90 sequence but not other Gly-Pro motif is required for the binding of CA protein to CypA. Therefore, CypA might be likely to act as a molecular chaperone but not a cis-trans isomerase (Zhao et al., 1997). However, one report showed that CypA does not only bind CA protein but also catalyzes efficiently cis-trans isomerization of Gly89-Pro90 peptideyl-prolyl bond (Bosco et al., 2002). The relationship between the Gly89-Pro90 bond and catalysis of cis-trans isomerization by CypA remains unclear.

It has been well established that CypA promotes an early step of HIV-1 infection in human cells (Franke et al., 1994; Thali et al., 1994; Braaten et al., 1996a; Franke and Luban, 1996; D’Souza et al., 2004). CypA is efficiently encapsidated into HIV-1 produced from infected cells through interaction with the CA domains of the Gag polypeptide and disruption of CypA incorporation into virions by CA or HIV-1 Gag mutants caused a decrease in replication efficiency (Franke et al., 1994; Thali et al., 1994; Ott et al., 1995; Braaten et al., 1996a; Bukovsky et al., 1997; Ackerson et al., 1998; Braaten and Luban, 2001). It is still unclear how CypA is efficiently packaged into HIV-1 virion, but several reports showed that both dimerization of CA and multimerization of CypA are required for efficient interaction (Colgan et al., 1996; Javanahishi et al., 2007). Although CA-CypA interaction is required for infectivity, the important point is that CypA interacts with incoming HIV-1 cores in newly infected target cells rather than during HIV-1 budding from the virion producer cells, indicating that target cell CypA promotes HIV-1 infectivity (Kootstra et al., 2003; Towers et al., 2003; Sodroski et al., 2004).

CypA-dependent virus replication is only limited to retroviruses which encode CA that binds CypA. In fact, only those retroviruses are dependent upon CypA for replication (luban et al., 1993; Franke et al., 1994; Thali et al., 1994; Braaten et al., 1996c; Franke and Luban, 1996). These observations suggested that CA–CypA interaction might contribute tropism determinants for retroviruses. HIV-1 infection in non-human primate cells is blocked prior to reverse transcription after virus entry (Shibata et al., 1995; Himathongkham and Luciw, 1996; Hofmann et al., 1999; Besnier et al., 2002; Cowan et al., 2002; Munk et al., 2002; Hatziantoniou et al., 2003; Towers et al., 2003). This restriction is thought to be the same step in the retrovirus life cycle where CypA works (Braaten et al., 1996b). Indeed, analysis of CypA-binding region of CA with chimeric viruses of HIV-1 and SIV showed the viral determinant for species-specificity (Shibata et al., 1991, 1995; Dorfman and Gottlinger, 1996; Bukovsky et al., 1997;
Sakuma and Takeuchi Receptor-independent SIV tropism

Human CypA is required for efficient HIV-1 infection but not SIV. There is no known role for CypA in SIV infection in human cells. Recently, the first report from the laboratory of Klaus Strebel showed that human CypA acts as restriction factor against the infection of two SIVs (SIVmac and SIVagm) in human cells, and Vif protein of two SIVs counteracts a CypA-imposed inhibition against the infection of two SIV strains with exclusion of CypA from SIV virion (Takeuchi et al., 2007). This phenomenon is different from the function of SIVagm Vif against hApo3G previously reported from the same laboratory (Takeuchi et al., 2005) because they used human cells lacking detectable deaminase activity.

Moreover, a recent report showed a species-specific effect of CsA, a peptidyl-prolyl cis-trans isomerase (PPIase) inhibitor, on SIV replication, implying a possible contribution of CypA to the determination of SIV tropism (Figure 1; Takeuchi et al., 2012). They demonstrated a host species-specific effect of CypA on SIV replication: CypA affects the replication of two SIVs (SIVmac and SIVagm) negatively in human cells but positively in macaque cells (Figure 1). Further analysis indicated that the infection of two SIVs was not significantly affected by CypA but inhibited by cyclophilin B (CypB), another PPIase, in human cells (Figure 2A; Takeuchi et al., 2012). In contrast, CypA is likely to have positive

![Figure 1](image1.png)

**FIGURE 1** A schema for the effect of CsA on HIV/SIV replication in human/macaque cells. (A) CsA treatment impairs the replication of HIV-1 (left panel) but enhances SIV replication (right panel) in human cells. (B) CsA treatment inhibits SIV replication in macaque cells. The solid line indicates virion accumulation of culture supernatant in the absence of CsA and the broken line indicates that of culture supernatant in the presence of CsA.

![Figure 2](image2.png)

**FIGURE 2** A schema for the effect of cyclophilin A and cyclophilin B on HIV/SIV replication in human/macaque cells. (A) CypA knock-down (CypA-KD) impairs the replication of HIV-1 (upper left panel). In contrast, SIV replication is not reduced but rather enhanced by CypA knock-down (upper right panel). CypB knock-down (CypB-KD) shows no significant effect on HIV-1 replication (lower left panel) but enhances the replication of SIV (lower right panel). (B) CypA-KD inhibits SIV infection. The solid line indicates virion accumulation of culture supernatant produced from normal cells and the broken line indicates that of culture supernatant produced from CypA or CypB knock-down cells.
Viral replication is modulated by host cell factors. Many of these factors function in a species-specific manner. On the other hand, there exist host factors that restrict viral replication. The anti-viral system mediated by some of these restriction factors, termed intrinsic immunity, which is distinguished from the conventional innate and adaptive immunity has been indicated to play an important role in making species-specific barriers against viral infection. As discussed in this review, we describe the current progress in understanding of such restriction factors against retroviral replication, especially focusing on TRIM5α and APOBEC whose anti-retroviral effects have recently been recognized. Additionally, we mentioned a host species-specific effect of Cyps including CypA and CypB on SIV replication. Such restriction factors would play an important role in determining species-specific barriers against viral infection.

ACKNOWLEDGMENTS

This work supported by a grant for Young Scientists of HIV/AIDS research from the Ministry of Health, Labor, and Welfare of Japan.

REFERENCES

Achong, B., Roy, O., Canen, J., and Krogstad, P. (1998). Cells with high cyclophilin A content support replication of human immunodeficiency virus type 1 Gag mutants with decreased ability to incorporate cyclophilin. J. Virol. 72, 383–388.

Ahmed, H., Sakuragi, J., Takeuchi, Y., Tomonaga, K., Kawamura, M., Fekara, S., Mura, T., Shanjo, T., and Hayami, M. (1992). Biological characterization of human immunodeficiency virus type 1 and type 2 mutants in human peripheral blood mononuclear cells. Arch. Virol. 123, 177–187.

Bertolla, L., Subianto, S., Sokolakaja, E., and Luban, J. (2004). HIV inhibition of human immunodeficiency virus type 1 is counteracted by factors that stimulate synthesis or nuclear translocation of viral DNA. J. Virol. 78, 11739–11750.

Bosman, C., Takeuchi, Y., and Tooyoo, G. (2002). Restriction of Lantavirus in macaques. Proc. Natl. Acad. Sci. U.S.A. 99, 11920–11925.

Bishop, K. N., Holmes, K. H., Shioda, A. M., Dommon, N. G., Cho, S. J., and Malim, M. H. (2004a). Cytidine deamination of retroviral DNA by diverse APOBEC proteins. Curr. Biol. 14, 1395–1399.

Bishop, K. N., Holmes, K. H., Shioda, A. M., and Malim, M. H. (2004b). APOBEC-mediated editing of viral RNA. Science 305, 645.

Blanc, D., Patou, C., Schütz, T. F., Weiss, R., and Sprey, R. (1991). Transcomplementation of Vif- HIV-1 mutants in CEM cells suggests that Vif affects late steps of the viral life cycle. Virology 193, 189–192.

Borgert, H. P., Dohle, B. P., War- ged, H. L., and Allen, R. K. (2004). A single amino acid difference in the host APOBEC3C protein controls the primate species specificity of HIV type 1 vision infectivity factor. Proc. Natl. Acad. Sci. U.S.A. 101, 3770–3774.

Borman, A. M., Quilliam, C., Charman, P., Ding, Q., and Clavel, F. (1995). Human immunodeficiency virus type 1 Vif: mutant particles from restricted cells: role of Vif in correct particle assembly and infectivity. J. Virol. 69, 2008–2007.

Bowen, D., A. M., Enomoto, E. F., Pochap- sisky, S., and Kien, D. (2001). Cyclin-dependent/cyclin immu- nization in native HIV-1 capsid by human cytoplasmic DNA. Proc. Natl. Acad. Sci. U.S.A. 98, 5247–5252.

Braaten, D., Abbot, C., Franke, E. K., Yin, L., Phans, W., and Luban, J. (1996a). Cyclosporine A-resistant human immunodeficiency virus type 1 variants demonstrate that HIV inhibits the functional target of cyclophilin A. J. Virol. 70, 5170–5176.

Braaten, D., Franke, E. K., and Luban, J. (1996b). Cyclophilin A is required for an early step in the life cycle of human immunodeficiency virus type 1 before the initiation of reverse transcription. J. Virol. 70, 3553–3560.

Braaten, D., Franke, E. K., and Luban, J. (1996c). Cyclophilin A is required for the replication of group M human immunodeficiency virus type 1 (HIV-1) and simian immunodeficiency virus SIVCPZGAG but not group O HIV-1 or other primate immunodeficiency viruses. J. Virol. 70, 4225–4227.

Braaten, D., and Luban, J. (2001). Cyclophilin A regulates HIV-1 infectivity. J. Virol. 75, 13001–13004.

Brennan, G., Kozyrev, Y., and Hu, S. L. (2010). Evolution of APOBEC family. journal.pone.0014019 doi: 10.1371/journal.pone.0014019.

Dang, Y., Wang, X., Esselman, W. J., and Zheng, Y. H. (2006). Rapid turnover and polyu-ribosylation of the retroviral restric- tion factor TRIM5. Virology 349, 300–315.

Dietrich, E. A., Jones-Engel, L., and Hu, S. L. (2010). Evolution of the antiretroviral restriction factor TRIM5α in Old World primates. PLoS One 5, e83089. doi:10.1371/journal.pone.00083089.

Downs, B. P., Schulze, A., and Callen, B. W. (2005). Human APOBEC3B is a potent inhibitor of HIV-1 infectivity and is resistant to HIV-1 Vif. Virology 356, 281–288.

Dorfman, Y., and Gottlinger, H. G. (1996). The human immuno-deficiency virus type 1 capsid p2 domain confers sensitivity to the cyclophilin- binding drug SDF 8174-81. J. Virol. 70, 5751–5757.

Fan, L., and Fudenberg, R. (1992). Cell- free transmission of Vif mutants of HIV-1. Virology 191, 19–29.

Fischer, G., Willmann-Lioubid, B., Lang, K., Kiehlau, T., and Schmid, A. C. (2009). Cyclophilin and peptidyl-prolyl cis-trans isomerase are probably identical proteins. Nature 337, 476–479.

Fisher, A. G., Ensal, B., Ivanoff, L., Chamberlain, M., Petteway, S. R., Ran- ton, L., Gallic, B. C., and Wong- Staal, F. (1987). The ser gene of HIV-1 is required for efficient virus transmission in vitro. Science 235, 888–893.

Franke, E. K., and Luban, J. (1996). Inhibition of HIV-1 replication by cyclophilin A or related compounds correlates with the ability to disrupt the Gag-cytoplasmic interaction. Virology 222, 279–282.
and Henderson, L. E. (1995). Analysis and localization of cyclophilin A found in the virions of human immunodeficiency virus type 1 MN strain. AIDS Res. Hiv Sci. 11, 1083–1096.

Owusu, C. M., Song, B., Perron, M. J., Yang, P. C., Stemmler, M., and Sodroski, J. (2004). Binding and susceptibility to postentry restriction factors in monkey cells are specified by distinct regions of the human immunodeficiency virus type 1 capsid. J. Virol. 78, 5427–5437.

Owusu, C. M., Song, P. C., Goulting, H., and Sodroski, J. (2003). Human and simian immunodeficiency virus capsid proteins are major viral determinants of early postentry restriction blocks in simian cells. J. Virol. 77, 725–738.

Pacinco, B., Fimini, A., Magon-Estrada, K., and Sodroski, J. (2009). Species-specific inhibition of foamy viruses from South American monkeys by New World Monkey foamy viruses: infectious particles with dual sensitivity to Fv-1 restriction. Proc. Natl. Acad. Sci. U.S.A. 106, 11487–11492.

Reit, A., Raab, S. V., Baun, R. H., Gerwin, B. L., and Duran-Troise, G. (1997). Photoinfective mixing between N- and B-tropic murine leukemia viruses in human cells. Proc. Natl. Acad. Sci. U.S.A. 104, 10176–10183.

Rina, A., Kim, K. S., Buarin, E., and Sodroski, J. (2004). TRIM5Delta mediates the postentry block to N-tropic murine leukemia viruses in human cells. Proc. Natl. Acad. Sci. U.S.A. 101, 5876–5879.

Rina, A., Kim, K. S., Buarin, E., and Sodroski, J. (2004). TRIM5Delta mediates the postentry block to N- and B-tropic murine leukemia viruses in human cells. Proc. Natl. Acad. Sci. U.S.A. 101, 10176–10183.

Rina, A., Kim, K. S., Buarin, E., and Sodroski, J. (2004). TRIM5Delta mediates the postentry block to N- and B-tropic murine leukemia viruses in human cells. Proc. Natl. Acad. Sci. U.S.A. 101, 10176–10183.

Rina, A., Kim, K. S., Buarin, E., and Sodroski, J. (2004). TRIM5Delta mediates the postentry block to N- and B-tropic murine leukemia viruses in human cells. Proc. Natl. Acad. Sci. U.S.A. 101, 10176–10183.

Rina, A., Kim, K. S., Buarin, E., and Sodroski, J. (2004). TRIM5Delta mediates the postentry block to N- and B-tropic murine leukemia viruses in human cells. Proc. Natl. Acad. Sci. U.S.A. 101, 10176–10183.
Zhang, H., Yang, B., Pomerantz, R. J., Zhang, C., Arunachalam, S. C., and Gao, L. (2003). The cytidine deaminase CEM15 induces hypermutation in newly synthesized HIV-1 DNA. Nature 424, 96–99.
Zhao, Y., Chen, Y., Schekowsky, M., Fischer, G., and Ke, H. (1997). Cyclophilin A complexed with a fragment of HIV-1 gag protein insights into HIV-1 infectious activity. Structure 5, 139–146.
Zheng, Y. H., Irwin, D., Tokunaga, K., Sata, T., and Peterlin, B. M. (2004). Human APOBEC3F is another host factor that blocks human immunodeficiency virus type 1 replication. J. Virol. 78, 6073–6076.

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 01 February 2012; accepted: 10 April 2012; published online: 27 April 2012.

Citation: Sakuma R and Takeuchi H (2012) SIV replication in human cells. Front. Microbiol. 3:162. doi: 10.3389/fmicb.2012.00162

This article was submitted to Frontiers in Virology, a specialty of Frontiers in Microbiology.

Copyright © 2012 Sakuma and Takeuchi. This is an open-access article distributed under the terms of the Creative Commons Attribution Non Commercial License, which permits non-commercial use, distribution, and reproduction in other forums, provided the original authors and source are credited.