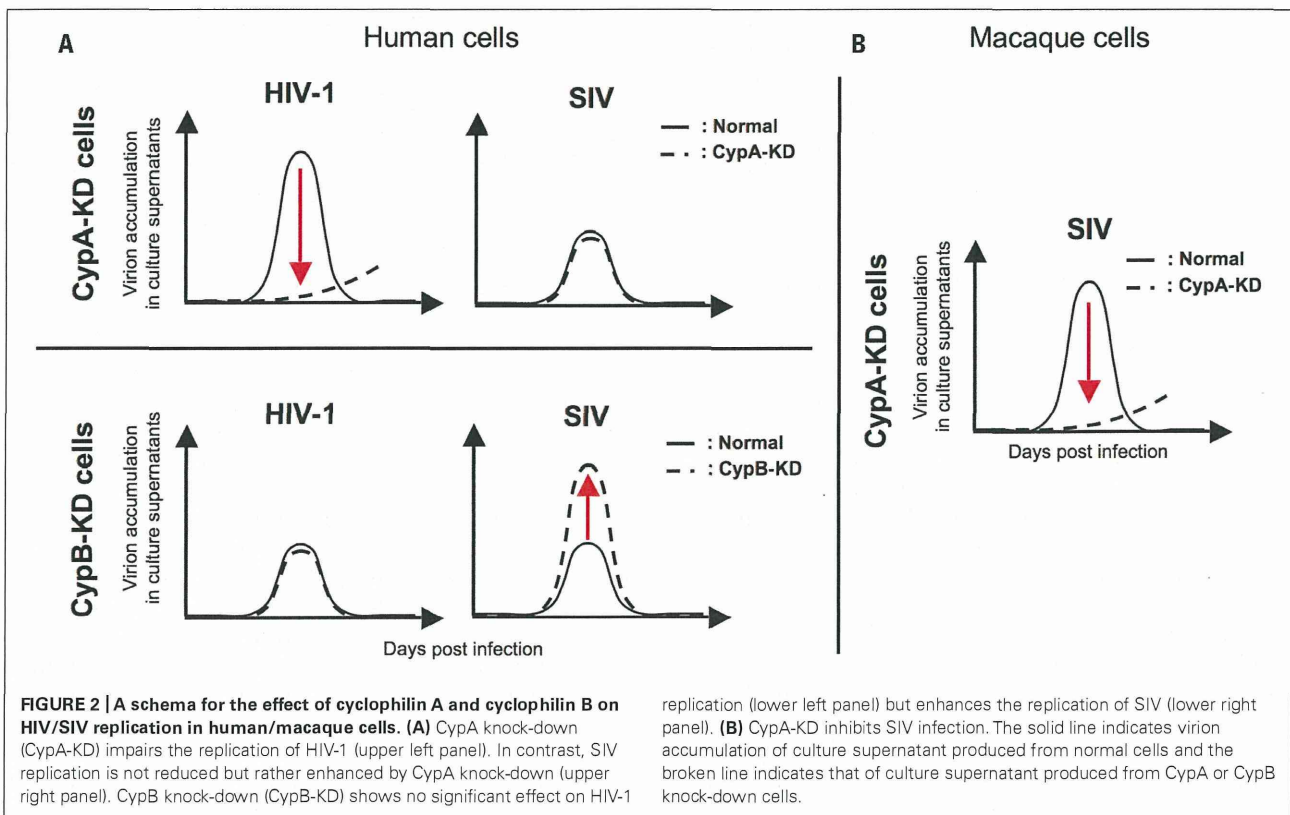


Cowan et al., 2002; Kootstra et al., 2003; Owens et al., 2003, 2004; Towers et al., 2003; Berthoux et al., 2004; Hatzioannou et al., 2004a, 2006; Ikeda et al., 2004; Sayah et al., 2004; Stremlau et al., 2004; Kamada et al., 2006).

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 Cyps 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



effects on the infection of two SIVs in macaque cells (Figure 2B; Takeuchi et al., 2012). These results suggest that Cyps might have a host species-specific effect of Cyps on SIV replication and provide insight into the mechanism of species-specific barriers against viral infection.

## CONCLUDING REMARKS

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 antiviral 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 TRIM5 $\alpha$  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.

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