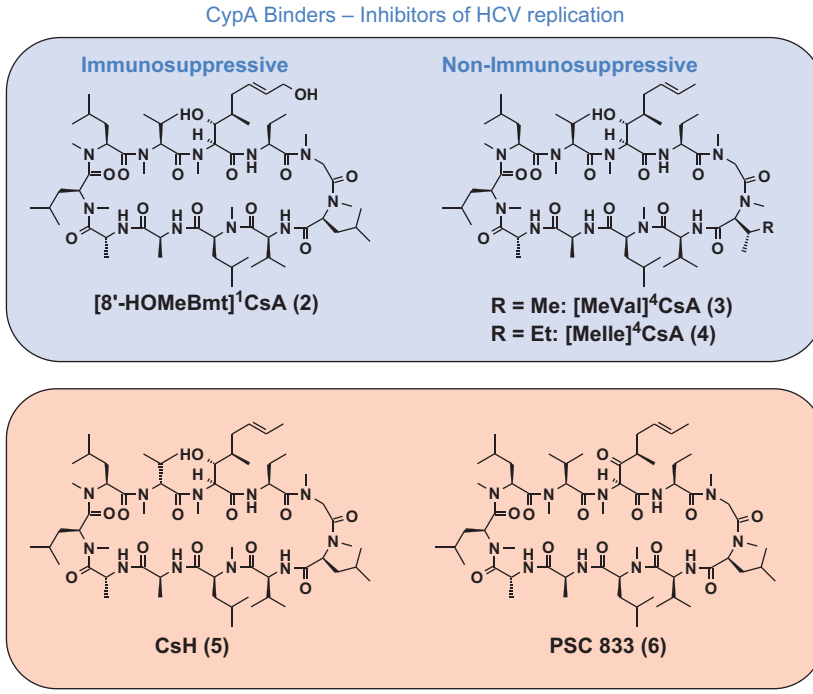

Figure 11.4 Immunosuppressive and non-immunosuppressive CsA derivatives are inhibitors of HCV replication whereas closely related analogs are devoid of CypA binding activity and do not inhibit HCV replication.

the assay. A structurally distinct Cyp inhibitor, sanglifehrin A, was also shown to be an inhibitor of HCV replication.[56]

Initial studies proposed CypB and/or CypC as being crucial to HCV replication;[56–58] however, other studies have suggested that CypA alone is crucial for HCV genotypes 1a, 1b and 2a.[59–63] To complicate matters, a more recent study suggests that several Cyps are important to various stages of HCV replication, including CypA (regulation of transcription and translation), CypB and CypC (protein conformation and transport), CypE and CypH (regulation of mRNA splicing, generation of host proteins necessary for HCV), Cyp40 (regulation of translation, non-vesicular transport of cholesterol, co-chaperone of Hsp90).[64] In any event, a recent consensus has emerged that CypA is likely the principal and perhaps exclusive Cyp crucial for HCV RNA replication and protein expression.[65,66]

There is ample evidence that the HCV life cycle is dependent on host cell Cyp for perhaps multiple processes, as is the case with HIV-1. A Cyp inhibitor, and in particular a CypA inhibitor that was non-immunosuppressive, would be an effective anti-HCV therapy.