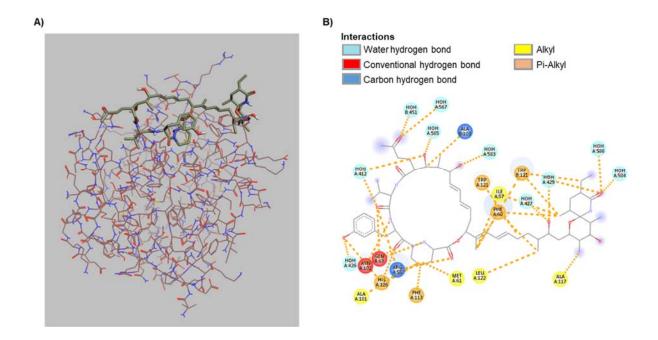


Supplementary Figure 1. Binding pattern of CsA (compound 1) in the CypA/calcineurin complex. A) A 3D diagram and B) a 2D diagram are depicted (PDB code: 1MF8). The docking process of 1 to the CypA/calcineurin complex was modeled using Flare and the resulting diagram was analyzed using the Discovery Studio Visualizer. CsA binds to the CypA/calcineurin complex via two parts of the ligand, and the red dotted line om (B) shows demarcation of CsA by CypA and calcineurin. P1, P2, P9, and P10 of CsA, as shown in Figure 4, mainly interact with CypA, whereas P4, P5, and P6 interact with calcineurin.



Supplementary Figure S2. Binding pattern of 21 (sanglifehrin A) to CypA. A) A 3D diagram and B) a 2D diagram are represented (PDB code: 1YND). The docking process of 21 to CypA was modeled using Flare and the resulting diagram was analyzed using the Discovery Studio Visualizer. Sanglifehrin A binds to a similar location within the active site of CypA, as CsA. The micro-cyclic ring contributes most to CypA binding and the long olefin tail (from C26) remains outside of the active site.