



STRUCTURAL
BIOLOGY

Volume 79 (2023)

Supporting information for article:

3D structures of the *Plasmodium vivax* subtilisin-like drug target SUB1 reveal conformational changes to accommodate a substrate-derived α -ketoamide inhibitor

Mariano Martinez, Fernando Batista, Manon Maurel, Anthony Bouillon, Laura Ortega, Anne Marie Wehenkel, Lucile Le Chevalier-Sontag, Arnaud Blondel, Ahmed Haouz, Jean-François Hernandez, Pedro M. Alzari and Jean-Christophe Barale

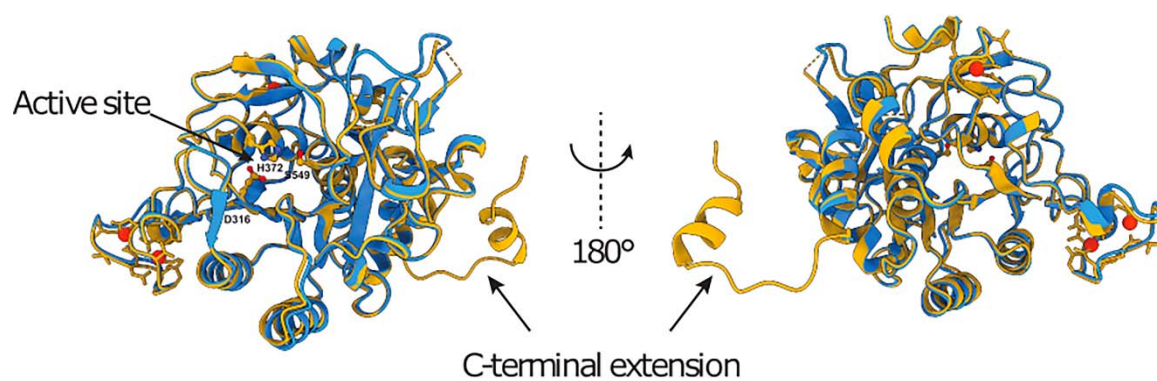


Figure S1 Superposition of the crystal structures of PvS1_{FL-bac} (blue, PDB 4tr2, residues Tyr₂₇₇-Lys₆₁₁) with PvS1_{Cat} (yellow) catalytic domains. The three main residues of PvS1 active site (D₃₁₆, H₃₇₂ and S₅₄₉) and calcium ions (in red) are shown.

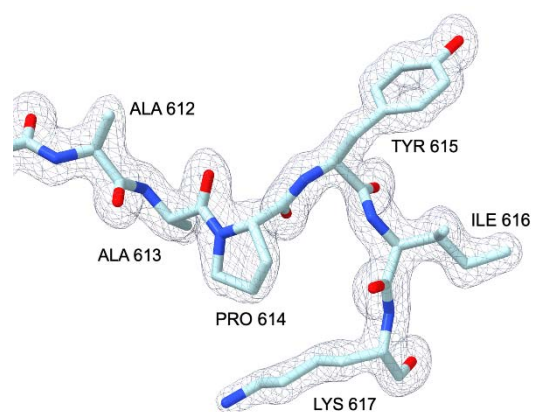


Figure S2 Electron density of PvS1_{Cat-Tryps} small C-terminal peptide extension 612-617 that is engaged in crystal contacts.

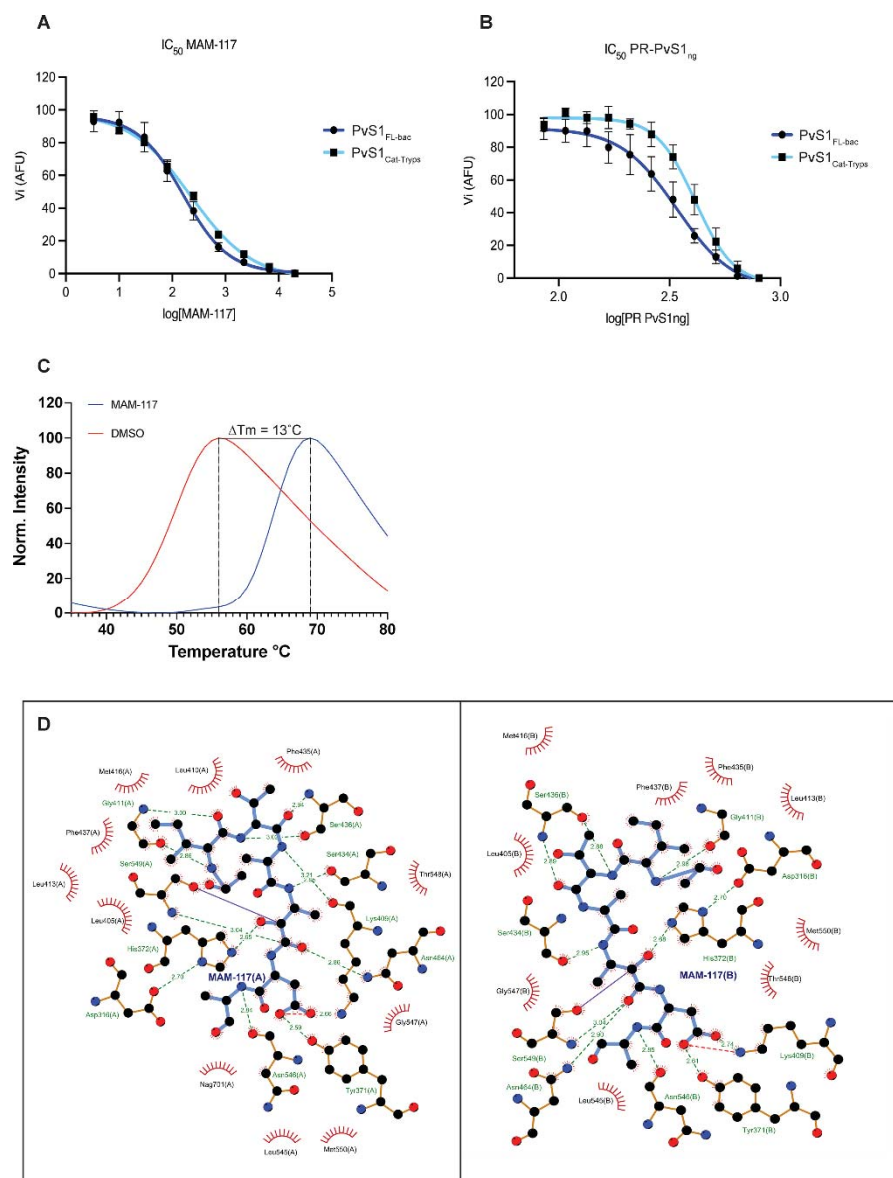
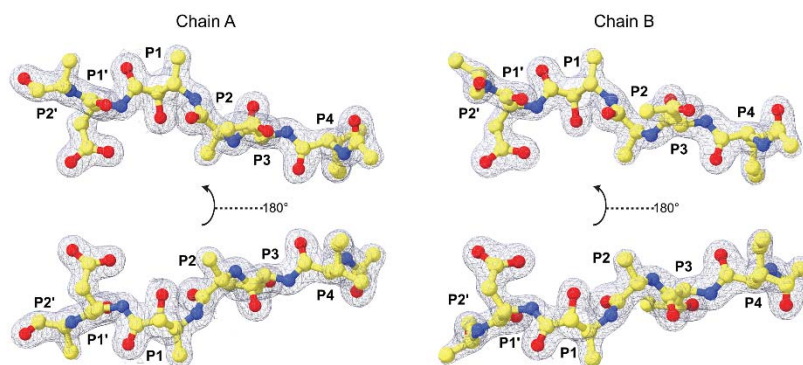
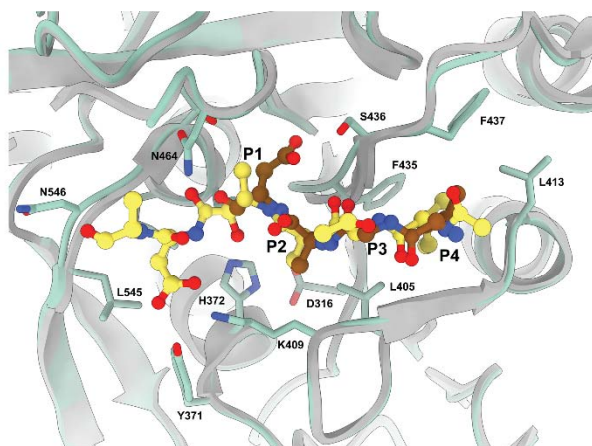


Figure S3 **A:** IC₅₀ determination of MAM-117 for recombinant PvS1_{FL-bac} (164.8 ± 27.3 nM) and PvS1_{Cat-Tryps} (225.5 ± 32.8 nM) active enzymes. **B:** IC₅₀ determination of PR-PvS1_{ng} pro-region for recombinant PvS1_{FL-bac} (325.9 ± 19.4 nM) and PvS1_{Cat-Tryps} (430.3 ± 40.3 nM) active enzymes. **C:** Melting temperatures (T_m) of PvS1_{Cat-Tryps} with DMSO or MAM-117 determined with the ThermoFluor assay.

A



B



C

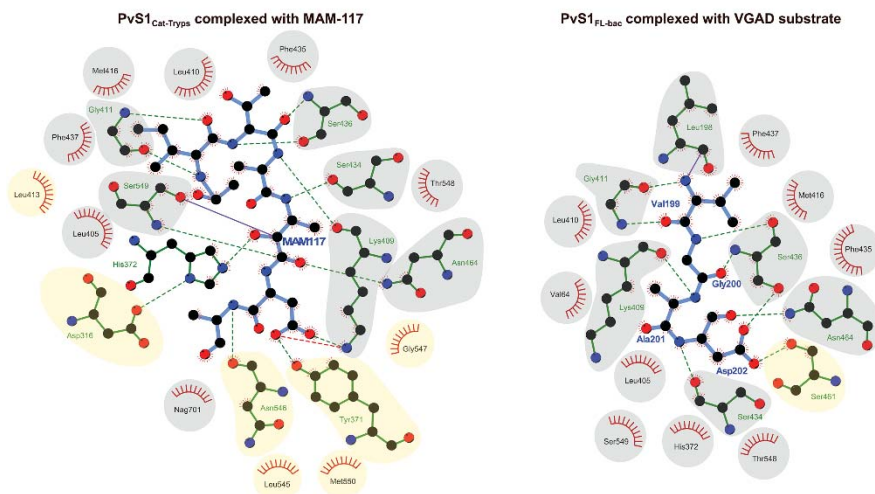


Figure S4 A: Electron density of the MAM-117 inhibitor present in chains A and B of the asymmetric unit, viewed at two different angles. B: Superposition of PvS1_{Cat-Tryps} (green) and PvS1_{FL-bac} (grey) crystal structures complexed with MAM-117 (yellow) or with PvS1 primary auto-maturation site (peptide V₁₉₉-G₂₀₀-A₂₀₁-D₂₀₂, brown). The P4-P1 positions of MAM-117 and PvS1 auto-

maturation site are indicated. **C:** Ligplot analysis showing the shared (in grey) or unique (in orange) interactions between PvS1 and MAM-117 (left panel) or PvS1 primary auto-maturation site (peptide V₁₉₉-G₂₀₀-A₂₀₁-D₂₀₂, right panel) from the complex crystal structures shown in (B).