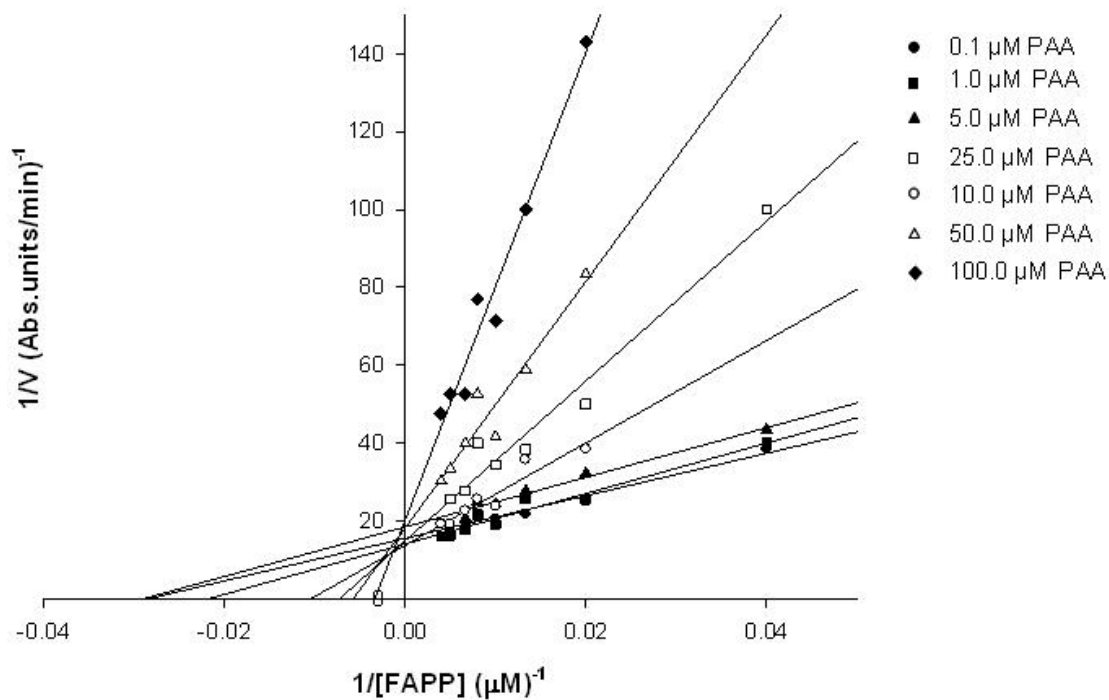


**Figure 1.** Tyr248 is found in two alternative conformations depending on the presence of substrates, substrate analogs or inhibitors at the active site. The “up” conformation is shown in black and corresponds to the unliganded bCPA1 (PDB code 1m4l) and the “down” conformation corresponds to the present structure (green traces) containing a PAA molecule at the active site (yellow sticks). The three Zn<sup>2+</sup> - coordinating residues are shown and labeled.



**Figure 2.** Double reciprocal plot for hCPA1 inhibition measured at seven different hCPA1/PAA ratios. Enzyme concentration was 5 nM, PAA concentrations ranged from 100 nM to 100  $\mu\text{M}$  and PAA concentrations are indicated in the figure. The calculated  $K_m$  value for the FAAP substrate is  $36 \pm 4$   $\mu\text{M}$  and the concentrations used ranged from 25 to 250  $\mu\text{M}$ . The experimental points shown are the mean of three repeated measurements

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hCPA1 LETFVGDQVLEIVPSNEEQIKNLLQLEAQEHLQLDFWKSPPTPGETAHVRVPFVNQAVKVFLESQGIAYSIMIEDVQVLL
bCPA1 KDFVGHQVLRITAADEAEVQTVKELEDLEHLQLDFWRGPGQSPIDVVPFSLQAVKVFLEAHGIRYRIMIEDVQSLL
*** * ** ** * ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** ** **
** ** * **
99
hCPA1 DKENEEMLFNRRRARSTDTFNYATYH LEEIYDFLDLLVAENPHLVSKIQIGNTYE RPIYVLKFSTGGKRPAIWIDTGI
bCPA1 DDEQEQMFASQSRARSTNTFNYATYHTLDDEIYDFMDLLVAEHP LVSKLQIGRSYEGRPIYVLKFSTGGSNRPAIWIDLGI
*x xx xxxxxxx xxxx
69 72 127 145
hCPA1 HSREWVTQASGVWFAKKITQDYQDAAFTAILDTLDIFLEIVTNPDGFAFTHSTNRMWRKTRSHTAGSLCIGVDPNRNWDA
bCPA1 HSREWITQATGVWFAKFTEDYQDPSFTAILDSMDIFLEIVTNPDGFAFTHSQNRLWRKTRSVTSSSLCVGDANRNWDA
*x xx *x
196
hCPA1 GF LSGASSNPCSETYHGKFANSEEVKSIVDFVKDHGNIKAFSIHSYSQLLMYPYGYKTEVPDPDQDELDQLSKAAVTAL
bCPA1 GFGKAGASSSPCSETYHGKYANSEEVKSIVDFVKDHGNFKAFLSHSYSQLLLYPYGYTTQSIPDKTELNQVAKSAVEAL
248 255 270
hCPA1 ASLYGTKFNYGSIIKAIYQASGSTIDWTYSQGIKYSFTFELRDTGRYGFLLPASQIIPTAKETWLALLTIMEHTLNHP-
bCPA1 KSLYGTSYKYGSIITIYQASGSIDWSYNQIKYSFTFELRDTGRYGFLLPASQIIPTAQETWLGVLTIMEHTLNNLY
xxx *x *x *x *x *x

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**Figure 3.** Sequence alignment of hCPA1 and bCPA1 zymogens coloured according to the computed ODA values. Position 99 indicates the last residue of the pro-domains; some other functionally important residues are labelled. An (x) identifies residues located at the interface with CTGC, while an asterisk (\*) labels the residues at the interface with PPE. The sequence of hCPA1 propeptide is shown in grey to indicate that its 3D structure has not been determined. The sequences corresponding to known 3D structures have been coloured with an in-house script according to ODA energy values from red (energy value < -10.0 kcal/mol) to blue (energy value = 0.0).