

# Implication of cysteine residues in the selection of oxorhenium inhibitors of cyclophilin hCyp18

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## Supplementary Information

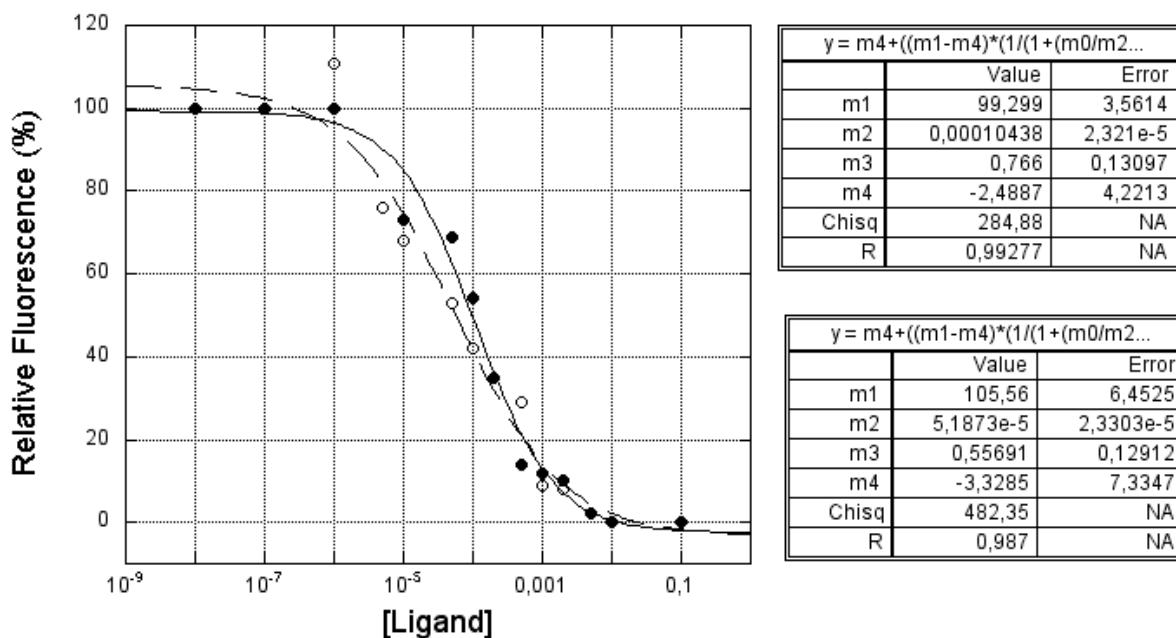
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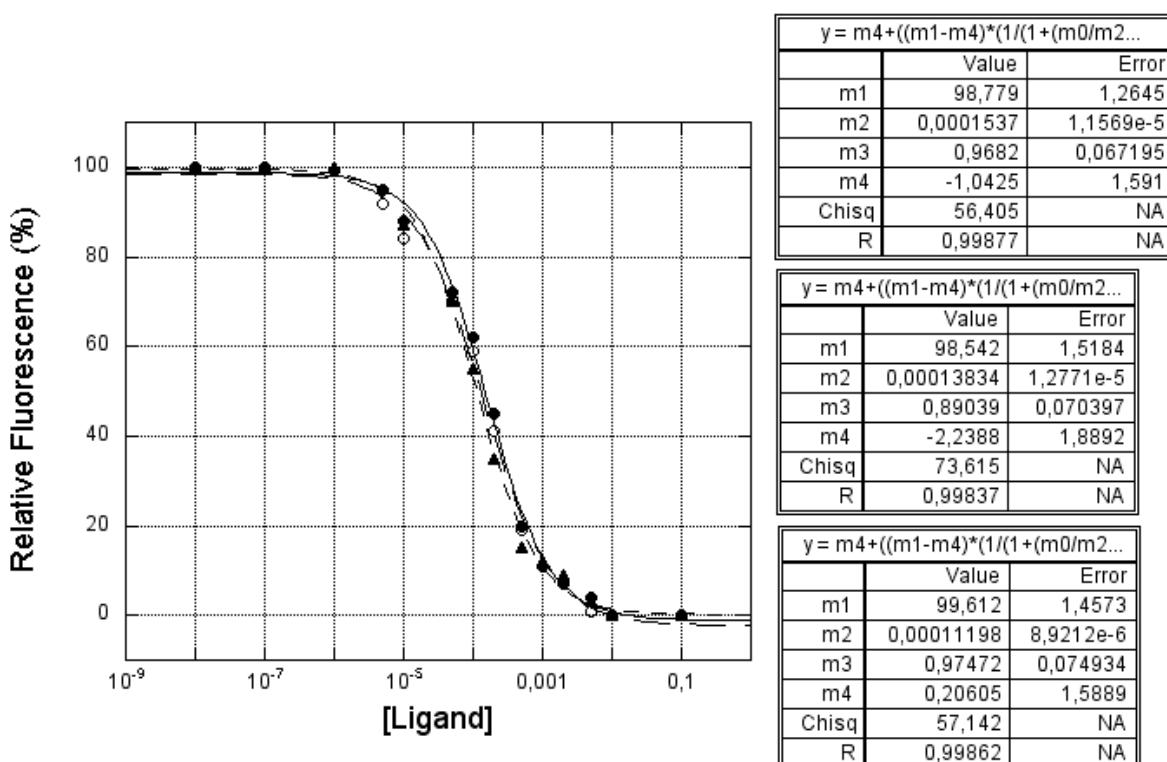
### ABBREVIATIONS:

Aac-*p*NA: amino acyl-4-nitroanilide; Acm: carbamidomethylated; CEE: cyclophilin enhancing effect; CsA: cyclosporine A; DMSO: dimethylsulfoxide; DTT: dithiothreitol; GSH: glutathione; IIC: integrated ionic current; Kd: dissociation constant; LC-ES/MS: liquid chromatography coupled to on-line electrospray mass spectrometry; NS<sub>2</sub>: N-bis(2-thioethyl); *p*NA: 4-nitroanilide; PPIase: peptidyl-prolyl isomerase; RP-HPLC: reverse phase high performance liquid chromatography.

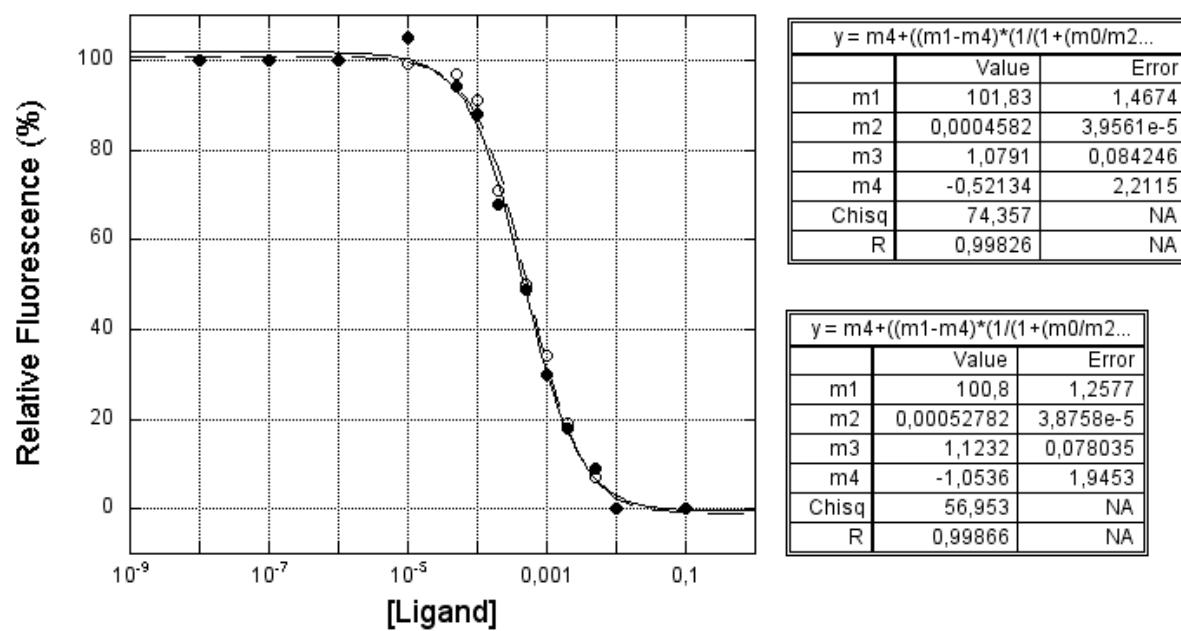
**Fig. S1:** Apparent Kds of module **10** (—●—) and of an equimolar mixture of modules **10** and **6** (—○—) (designated as ‘Ligand’).



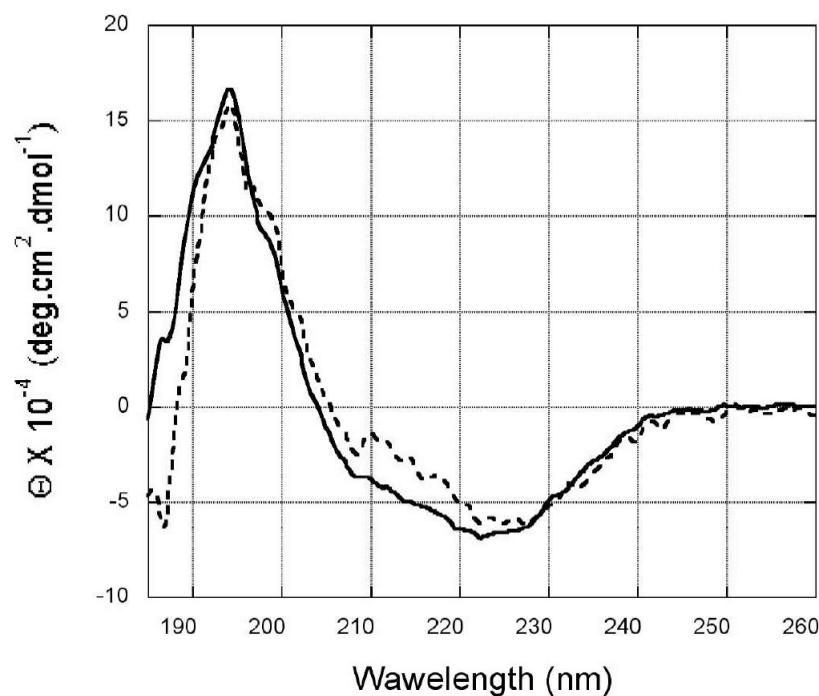
**Fig. S2:** Apparent Kds of module **11** (—●—) and of an equimolar mixture of modules **10** and **7** (—○—) and modules **10** and **8** (---▲---) (designated as ‘Ligand’).



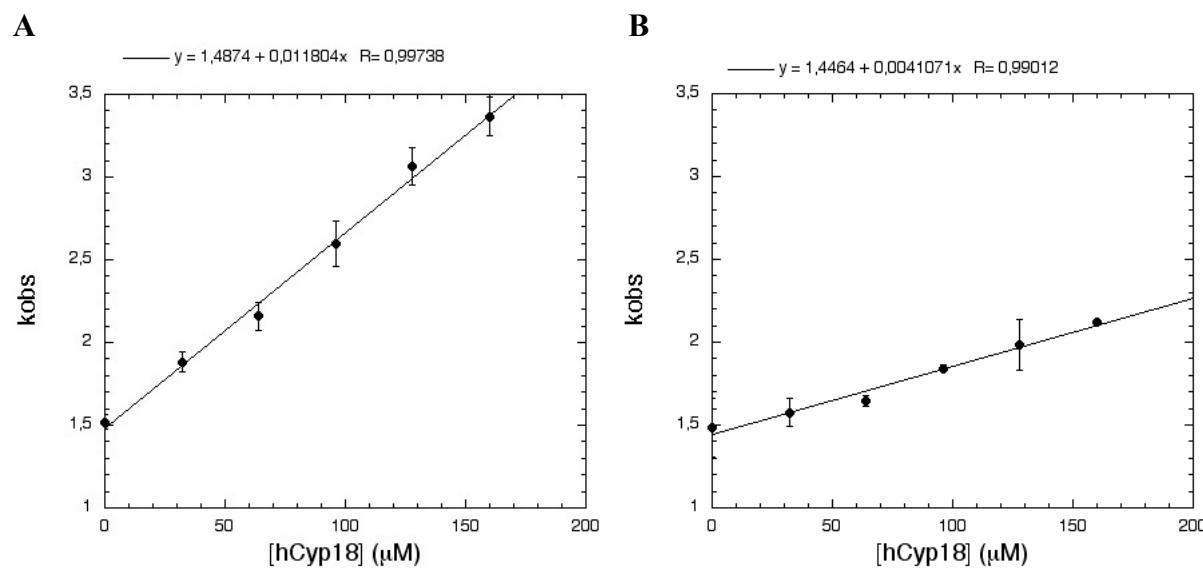
**Fig. S3:** Apparent Kds of module **12** (—●—) and of an equimolar mixture of modules **12** and **9** (—○—) (designated as ‘Ligand’).



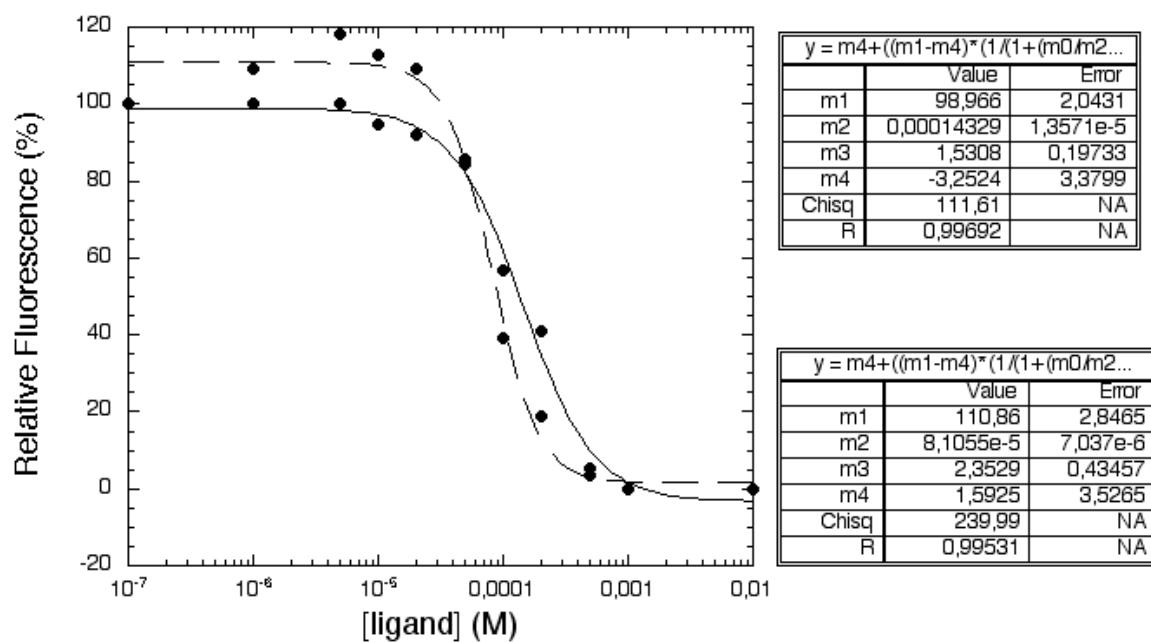
**Fig. S4:** Circular dichroism spectra of 10  $\mu$ M native hCyp18 (—) and 10  $\mu$ M Acm<sub>2</sub>-hCyp18 (---) in water at 20 °C.



**Fig. S5:**  $k_{obs}$  of hCyp18 (A) and Acm<sub>2</sub>-hCyp18 (B) calculated from the trypsin-coupled PPIase assay using Suc-Ala-Ala-Pro-Arg-pNA as a substrate.



**Fig. S6:** Affinity constants Kd of Suc-Ala-Ala-Pro-Arg-pNA determined using the fluorescence quenching assay for hCyp18 (—●—) and Acm<sub>2</sub>-hCyp18 (—○—).



**Fig. S7:** Affinity constants Kd for Acm<sub>2</sub>-hCyp18 of complexes **1** (—▲—) and **2** (— -△- —) determined using the fluorescence quenching assay.

