

Supporting information

Identification of small molecules disrupting the ubiquitin proteasome system in malaria

Lydia Mata-Cantero¹, María Jesús Chaparro¹, Gonzalo Colmenarejo^{1,2}, Concepción Cid¹, Alvaro Cortes Cabrera¹, Manuel S. Rodriguez³, Julio Martín¹, Francisco Javier Gamo¹ and Maria G. Gomez-Lorenzo^{1,#}

¹Tres Cantos Medicines Development Campus, Diseases of the Developing World. GlaxoSmithKline. Severo Ochoa 2, Tres Cantos 28760, Madrid, Spain.

²Current address: IMDEA Food, Biostatistics and Bioinformatics Unit. Ctra Cantoblanco 8, 28049, Madrid, Spain

³ITAV, Université de Toulouse, CNRS and IPBS, Université de Toulouse, CNRS. 1 place Pierre Potier, Oncopole entrée B, 31106 Toulouse, France.

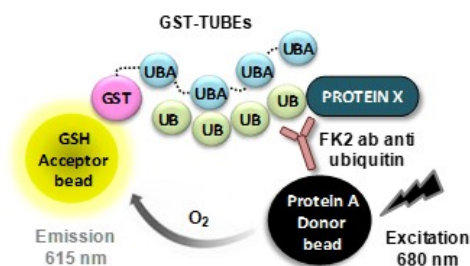
#Corresponding author

Table of Contents

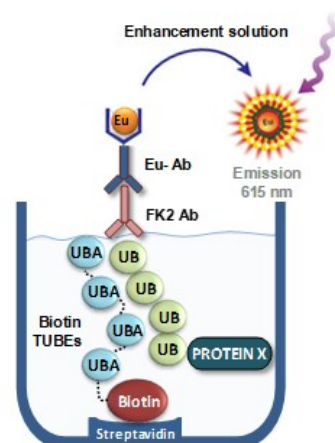
- Supplementary Figure 1. Progression cascade for the HTS	S2
- Supplementary Table 1. Results for non selective proteasome inhibitors	S3
- Supplementary References	S5

Supplementary Figure 1. Progression cascade for the HTS. (A) Schematic representation of the two assays used to triage compounds.¹ (B) Progression cascade of the screening with the number of compounds selected and selection criteria for each of the steps.

A



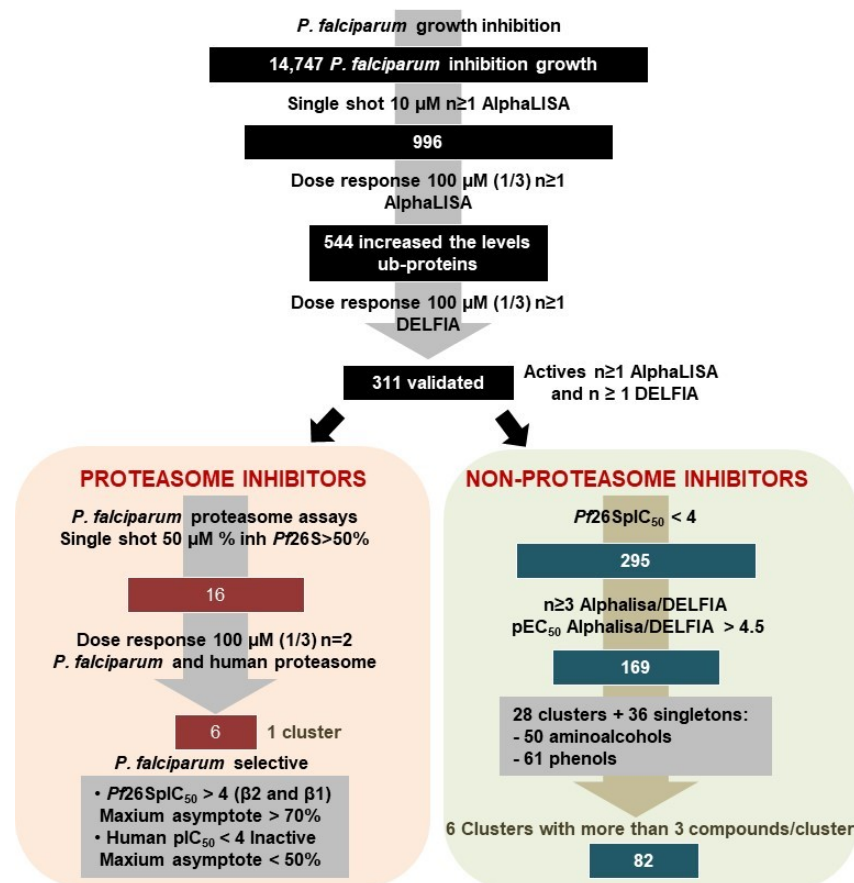
AlphaLISA



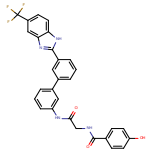
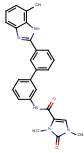
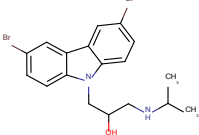
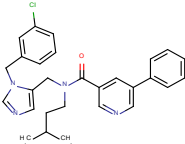
DELFLA

B

UPS SCREENING CAMPAIGN



Supplementary Table 1. Results for Non Selective Proteasome Inhibitors. Non-selective proteasome inhibitors identified in the study. Results in AMC assay for human THP1 and *P. falciparum* samples are shown.

Compound	Structure	Reported pEC50 whole cell 3D7A ¹⁸	Proteasome activity assays						Selectivity index		
			pIC50 THP1			pIC50 <i>P. falciparum</i>			$\beta 5$	$\beta 1$	$\beta 2$
			$\beta 5$	$\beta 1$	$\beta 2$	$\beta 5$	$\beta 1$	$\beta 2$			
TCMDC-136816		5.98	4.85	4.72	4.34	4.51	4.51	4.57	-0.34	-0.21	0.23
TCMDC-137137		6.30	4.41	4.53	4.36	4.30	4.28	4.22	-0.12	-0.25	-0.14
TCMDC-124100		6.35	<4	4.38	<4	4.34	<4	<4	0.34	-0.38	0.00
TCMDC-132465		6.12	<4	4.27	<4	4.59	<4	<4	0.59	-0.27	0.00

Supplementary References

(1) Mata-Cantero, L.; Cid, C.; Gomez-Lorenzo, M. G.; Xolalpa, W.; Aillet, F.; Martin, J. J.; Rodriguez, M. S. Development of two novel high-throughput assays to quantify ubiquitylated proteins in cell lysates: application to screening of new anti-malarials. *Malar. J.* **2015**, *14*, 200