Title: Histone deacetylase inhibitors with high in vitro activities against *Plasmodium falciparum* isolates collected from Gabonese children and adults

Authors: Erik Koehne ^{a,b*}, Andrea Kreidenweiss ^{a,b*}, Rella Zoleko Manego^{b,c}, Matthew McCall^b, Ghyslain Mombo-Ngoma^{b,c}, Marcel Karl Walter Mackwitz^d, Finn K. Hansen^d, Jana Held^{a,b}

Author Affiliations:

^a Institute of Tropical Medicine, University Hospital Tübingen, Wilhelmstrasse 27, D-72074 Tübingen, Germany;

^b Centre de Recherches Médicales de Lambaréné, B.P. 242, Lambaréné, Gabon;

^c Department of Tropical Medicine, Bernhard Nocht Institute for Tropical Medicine & I. Dep of Medicine, University Medical Centre- Hamburg-Eppendorf, Bernhard-Nocht-Strasse 74, D-20359 Hamburg, Germany;

^d Institute of Pharmacy, Medical Faculty, University of Leipzig University, Brüderstrasse 34, D-04103 Leipzig, Germany

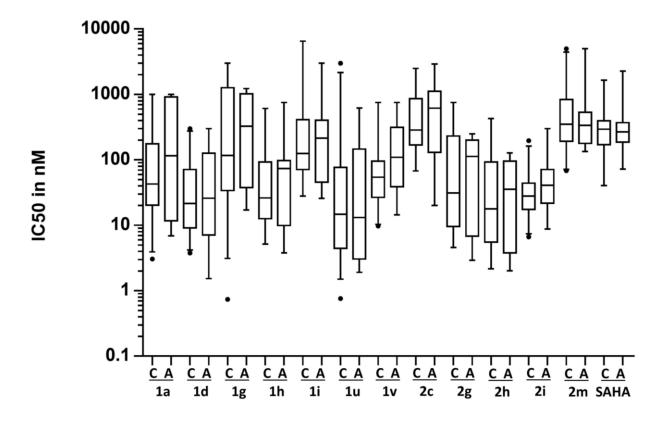
*These authors contributed equally to this work

$$R^1$$
 R^3
 R^3
 R^3
 R^2
 O
 O
 O
 O
 O

Compound ID	\mathbb{R}^1	\mathbb{R}^2	\mathbb{R}^3
1a	t-Bu	3,4-Me-Ph	Н
1d	t-Bu	4-Me ₂ N-Ph	Н
1g	c-Hex	1-Naphthyl	Н
1h	c-Hex	4-Me ₂ N-Ph	Н
1i	c-Hex	3,5-Me-Ph	Н
1u	c-Hex	4- <i>i</i> -Pr-Ph	Н
1v	n -Bu	4-Me ₂ N-Ph	Н
2c	c-Hex	4-Me ₂ N-Ph	Me
2g	Bn	4- <i>t</i> -Bu-Ph	Н
2h	Bn	4- <i>i</i> -Pr-Ph	Н
2i	Bn	4-Me ₂ N-Ph	Н
2m	4-F-Bn	3,5-Me-Ph	Н

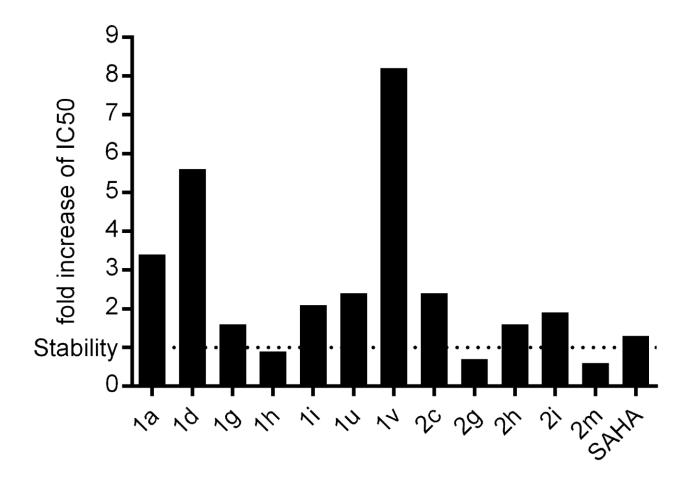
Supplementary Figure 1: Chemical structures of tested compounds

Chemical structures have already been published ^{5,6}



Supplementary Figure 2: Distribution of IC50 values

Distribution of IC50 values of HDACi candidates against *P. falciparum* isolates obtained from children (C) and adults (A). SAHA: suberoylanilide hydroxamic acid (Vorinostat). Box plots show median IC50 and 25% and 75% quartiles, respectively. Whiskers extend to the 5th and 95th percentiles. Dots outside the whiskers are outlier IC50 values.



Supplementary Figure 3: Stability of HDACi candidates

Fold increase of IC50 at study end determined in *P. falciparum* 3D7. Fold increase (IC50 at study end/IC50 at study start) of 1 represents stability of compound at study end.