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ERRATUM

Erratum to: Chemical profiling of deoxyhypusine hydroxylase inhibitors for antimalarial therapy

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Abstract A first approach to discover new antimalarials has been recently performed in a combined approach with data from GlaxoSmithKline Tres Cantos Antimalarial Set, Novartis-GNF Malaria Box Data set and St. Jude Children's Research Hospital. These data are assembled in the Malaria Box. In a first phenotypic forward chemical genetic approach, 400 chemicals were employed to eradicate the parasite in the erythrocytic stages. The advantage of phenotypic screens for the identification of novel chemotypes is that no a priori assumptions are made concerning a fixed target and that active compounds inherently have cellular bioavailability. In a first screen 40 mostly heterocyclic, highly active compounds (in nmol range of growth inhibition) were identified with EC50 values $\leq$2 μM against chloroquine-resistant *Plasmodium falciparum* strains and a therapeutic window $\geq$10 against two mammalian cell lines. 78 % of the compounds had no violations with the Lipinski Rule of 5 and only 1 % of the compounds showed cytotoxicity when applied at concentrations of 10 μM. This pre-selective step of parasitic eradication will be used further for a test of the Malaria Box with a potential in iron chelating capacity to inhibit deoxyhypusine hydroxylase (DOHH) from *P. falciparum* and *vivax*. DOHH, a metalloprotein which consists of ferrous iron and catalyzes the second step of the posttranslational modification at a specific lysine in eukaryotic initiation factor 5A (EIF-5A) to hypusine. Hypusine is a novel, non-proteinogenic amino acid, which is essential in eukaryotes and for parasitic proliferation. DOHH seems to be a "druggable" target, since it has only 26 % amino acid identity to its human orthologue. For a High-throughput Screening (HTS) of DOOH inhibitors, rapid and robust analytical tools are a prerequisite. A proteomic platform for the detection of hypusine metabolites is currently established. Ultra performance Liquid Chromatography enables the detection of hypusine metabolites with retention times of 7.4 min for deoxyhypusine and 7.3 min for hypusine. Alternatively, the analytes can be detected by their masses with gas chromatography/mass spectrometry or one-dimensional chromatography coupled to mass spectrometry. Moreover, the identified hits will be tracked further to test their efficacy in novel "in vitro assays". Subsequently in vivo inhibition in a humanized mouse model will be tested.

Keywords Deoxyhypusine hydroxylase · Phenotypic screening · DOHH inhibitors · Malaria · Hypusine

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