

Notes of Malaria *Libre* 2nd project meeting

12th August 2020; 1530-1630(Indian Standard Time)

Participants: Sanjay Batra, Kishore Mohan, PP Yadav, Niti Kumar (CDRI, India); Shailja Singh (JNU, India); Shridhar Narayan (FNDR, India); Gloria Serra (Dept. of Chemistry, Uruguay); Ram Singh(Delhi Technological University, India); R Venkatramanan (EDDC, Singapore); Clint Veale(South Africa); Sumbal Saha (UFSC, Brazil), Matt Todd(UCL, UK); Surajit Sadhukhan; Abhijit Kundu(TCGLS) and Kirandeep Samby (MMV, India)

Discussion points:

Early lead criteria for progressing the project to next stage was discussed

Based on the work flow, 1-2 mg of compounds synthesised in individual labs will be sent to TCGLS for screening in 3D7 LDH assay and HepG2 assay. Based on the activity, further screening cascade will be followed

Project challenges and way forward strategy was discussed

There were a few suggestions:

Will be good to have TCGLS provide a common intermediate for further synthetic work. It was highlighted that this strategy is in place and some intermediate was already provided to CDRI

Screen compounds in resistant cell lines available within the MMV network to identify MoA – it was explained that one representative compound from aryl imidazole scaffold was screened and is not cross-resistant in those cell lines. Further detailed profiling for representative potent compounds will be done. Shailja and Niti will help with additional studies to understand MoA. A separate discussion will be organized before the next project meeting

Sumbal will share the representative compounds to see if those align to our current scaffolds and will be worth screening for antimalarial activity

Pb liver stage activity can also be done at CDRI for the front runners

Contributions by new members:

Clint, Venkat and Ram will have a look at the detailed SAR and list of compounds to be synthesized and come back with suggestions before the next project meeting in 1st week of September

Sumbal will talk to the lab head for possible synthetic chemistry contribution

Action Items:

Synthesis of compounds – CDRI, TCGLS and Gloria

Screening of compounds – TCGLS and CDRI

Selection of compounds for assay synchronization (3D7 SYBR) at CDRI – Kiran to send two representative compounds to CDRI: Aryl piperazine: MMV024408 and MMV1803899; Aryl imidazole: MMV1804344 and MMV1804317 - **Done**

Screening in extended panel of strains and ring survival assay: Kiran to send the above compounds to Shailja

Screen representative compound from aryl piperazine analogs in panel of resistant cell lines – Kiran to send