**MedChem mPPase meeting Friday, June 9th 2016 at 12:00-13:30**

* Ainoleena, Henri, Keni, Alexi, Gustav, Jari and Niklas were present.
* No agenda – general updates i.e. what has been and/or needs to be done, manuscript.
* Henri had gotten an Academy of Finland grant (Novel protozoan inhibitors through structure- and fragment-based drug discovery approaches) 01.09.2017 - 31.08.2021
  + Screening of I/Br containing cmpds
    - FIMM ~55000 cmpds
    - Pittsburgh collaboration
    - assay/screening service, FIMM, 6 months
    - Henri and Keni will have a meeting with FIMM (~within a year) – price, possibilities
* Open screening program (Arto) – Erik/Jari purity/identity of cmpds to submit
* Keni’s autumn plans
  + start working with insect parasite cells since *E. choli*  didn’t turned out to be successful
  + refining the X-ray structure
  + cpm assays
  + cysteine binding tried but was not successful
  + retesting of cmpds starting from the ones from October 2016
    - New person to be hired? or Violet might assist with the testing
* Aino – TmPPase assay overview
  + Fluctuations in the results October 2016 to April 6th 2017 due to pipetting issues, Daniel’s short lab experience, reagent issues etc.
  + Pipetts calibrated, fresh protein, positive controls and Keni doing the testing seems that the method is consistent ☺
  + Independence of experiments? Two experiments with triplicates, well rather one experiment with six replicates since same solutions were used (same stock would have been fine, but more or less all the rest should have been new) However, not necessary to retest at the moment, maybe best cmpds at a later stage if required
* Niklas – Results from inhibition testing April 11th
  + MTI73 (old) couldn’t be retested but the resynthesized one was, also the ester
    - drop in activity for the MTI73 resynthesized one, although more pure according to NMR & MS
  + MTI55, the resynthesized one, it’s analogue (N-O flip) – the old one still shows inhibition, the new ones not as much
  + Most of the MTI cpmds synthesized/one step left(2cmpds)/purchased to be retested
  + Working on halogenated analogues of MTI55/73 – 3,5-dibromo, 3-bromo-5-methyl
    - will consider to make monosubstituted methyl/*t*-butyl analogues as well
* Gustav – 13 Ambinter isoxazoles from first screening
  + issues with the acid group being cleaved of during MS – might have been more pure cmpds as previously expected
    - 4 pure, 5 with various purity, 4 impure
* Manuscript – Discovery of membrane-bound pyrophosphatase inhibitors with *ex vivo* antiparasitic activity against *Plasmodium falciparum* using sequential rounds of screening
  + 1st batch of results – screening and SAR + mechanism of action
  + Henri had already an initial version of the manuscript that will be sent to everybody involved before the summer
    - If start writing now, then maybe published within a year or so…
  + Focus on
    - some important cmpds that need to be characterized properly by at least to methods + >95 % pure (for the rest identity/purity should be fine for supporting information)
    - mechanism of action of 2–3 cmpds
  + Summer/Late autumn
    - collect data -> choose cmpds -> repurchase/retest (<10) -> …
  + Sulphon space studied by Aaron, added value
* Keni will do the restesting in end of July 2017 using the DMSO stocks of the cmpds that he have of the 16+48 cmpds
  + New cmpds for testing later e.g. 18 Ambinter, remaining DAP, new NJ/AKI
* Niklas and Alexi will check the purity of the MS when data is available
* This document was written by Niklas and a copy has been put on E-Duuni.