**mPPase MedChem meeting 24.11.2016**

Present: HX, AT, NJ, JYK

**Actions from last meeting**

- Nephelometer tests for 18 compounds using detergent

* Concentrations 1µM, 5µM and 20 / 50 µM (depending on solubility)
* 10 azulenes + 6 Hit2Lead compounds + 2 controls (MTI-61 and AKIXVII103)
* With this setup, azulenes don’t aggregate (except those with indole / benzimidatsole in R2)

- P. Falciparum tests successful for two compounds (ex vivo IC50s of 8 µM and 18 µM)

* Testing with efflux inhibitors in future discussed

- L. Donovani tests

* Compounds are sent, same set than tested in P. Falciparum + Amb1761587 (best bromine) and Amb16561891 (best sulphonamide)

- 6 (Hit2Lead) +10 (benzazulene) new compounds tested

* Preliminary results in line with the previous ones, needs to be retested though after pipette re-calibration

- Progress on solving TL2-73 structure?

* Process ongoing

**To do**

- Asking Paula about TL2-73 analogues

* AK has promised to ask

-Verifying identity of the purchased compounds agreed to be important

* LC-MS for all purchased compounds (currently ~45 🡪 1200 €)
* HX says he can pay, tries to get AG to share the costs

- Nephelometer tests in future

* Need for aggregation testing discussed 🡪 Agreed that just active compounds are tested now, but in the future all new compounds will be tested
* Test conditions and other practicalities will be discussed in the next meeting (on Dec 9th)

- Next meetings

* Med Chem meeting December 9th at 10, place 3045c
* Full project meeting
  + Suggestion: in Leeds in February – early March 2017, AT makes a Doodle poll of dates
* GB + HX + JYK meetings concerning:
  + Packaging the med chem stories
  + Discuss with Adrian about experiments with TL2-73
  + Connect to industry (GSK?)
  + Connect to existing EU project / build a consortium 🡪 COST action representative briefly discussed

**Current plans**

**NJ**

* 11 analogues in progress, testing them, then deciding next bunch
* Exploring
  + R3 CN
  + R5 Et
  + O-N and N-N at the ring
  + Symmetric compounds with 2 units
* Could be explored
  + R5 further (only H and Et so far) – e.g. GB’s ideas of N-acylhydrazones
  + Isoxazole ring 🡪 e.g. isothiatzole
  + R2 + R4 (t-butyl and Me so far)

**AK**

* Discussed in the meeting on Dec 9th

**AT**

* Combine existing data (structure, docking, SARs, designs) to suggest a new hit list of ~40-50 compounds to be tested in the spring
  + Pharmacophore-based screen / analogues of the designs
  + JYK promised a budget of max EUR 3000
* Screen the Pittsburg library for Br/I derivatives
  + Accession of compounds to us in progress, HX
* QSAR can be started when data quality has been verified

**Other plans**

* Could be explored:
  + PPi analogues, artemisinin + mPPase (active in parasites, mode of action not known)
  + Penicillin etc. + mPPase (phosphate binding site + bioisosterism)