Malaria drugs

- Malaria is a high-impact disease that causes 300-500 million clinical cases and kills over a million persons annually
- Malaria vaccine initiatives have mostly had very low success rates, and drug resistance is spreading quickly
- Suitable new drug target proteins and lead chemical compounds are urgently needed
- None of the currently-used pharmaceuticals has originated from a de novo approach based on rationally-selected targets
- The completion of the Plasmodium falciparum genome sequence sparked great hope for the identification of new and novel drug targets and lead compounds, but so far, this has not really led to the exploitation of any new successful drug targets
Rational target and lead discovery

• A resource was needed for the rational selection of putative target proteins and lead compounds against malaria
• A system was designed to integrate protein data from the major malaria species, the human host and the mosquito host together with chemical data
• Data useful for drug discovery may include:
  • Activity
  • Functional and structural motifs
  • Ontology terms
  • Orthology information
  • Metabolic pathway information
  • 3D structural information
  • Drugability information
  • Ligand information
  • Literature information

Rational target and lead discovery

• Version 1 of the system was developed in Python / TurboGears / MySQL
• Version 2 is a complete rewrite in Java / NetBeans / MySQL
• Public data is combined and integrated with in-house analyses
• Drug trial information is linked to proteins and chemical compounds
Acknowledgements

- Jeanré Smit (Developer)
- Phele Mpangase (MSc student)
- Michal Szolkiewicz (MSc student)
- Misha le Grange (MSc student)
- John Overington and Louisa Bellis (EBI - ChEMBL)

Funding