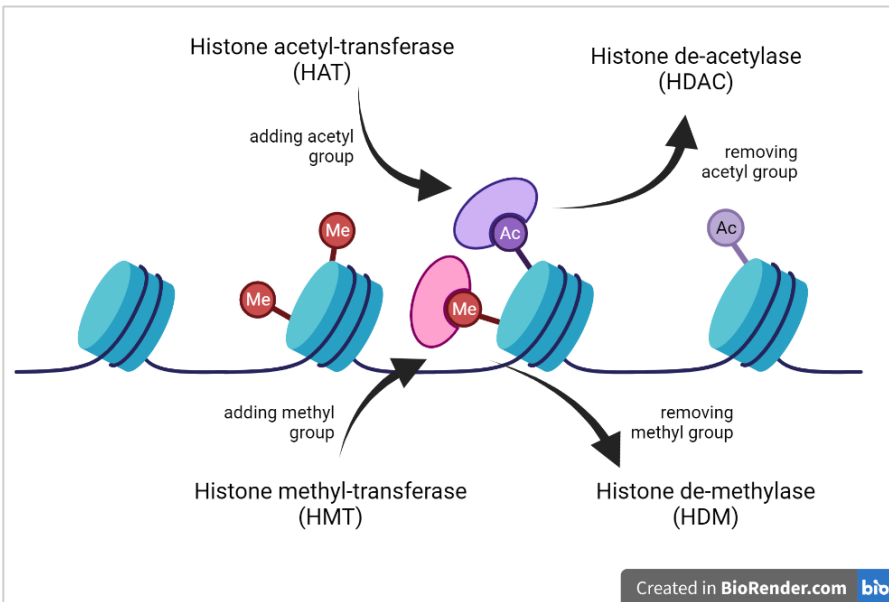


Histone modification enzyme inhibitors (HMEis) as novel flukicides.

Poster: Sarah Davey. Supervisors: Karl Hoffmann, Iain Chalmers, Aaron Maule.

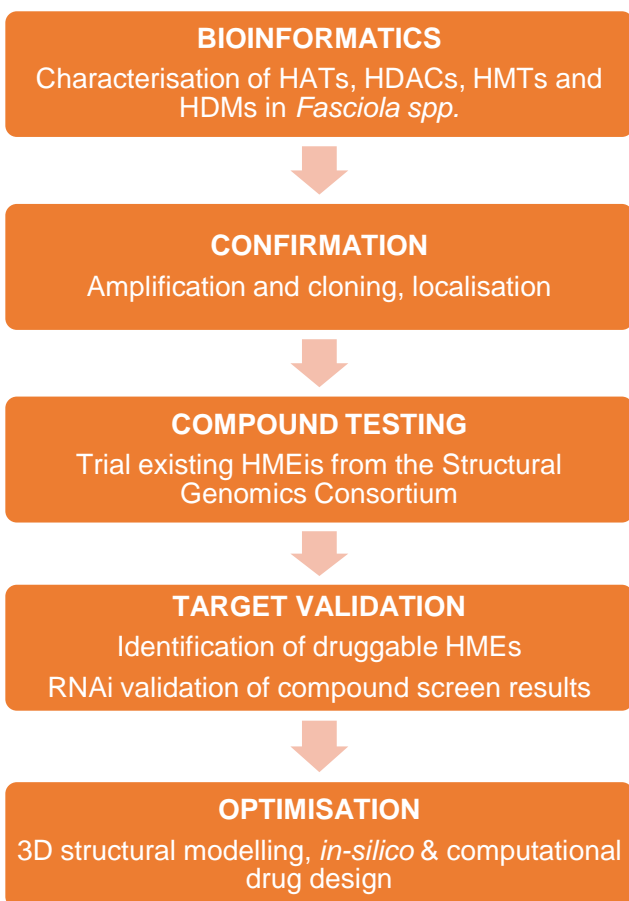


This project is currently focussed on two HME families – HAT/HDACs (acetyl-group modification) and HMT/HDMs (methyl-group modification). Further investigation of other HME families may occur depending on the outcome of preliminary investigations.

Project Background

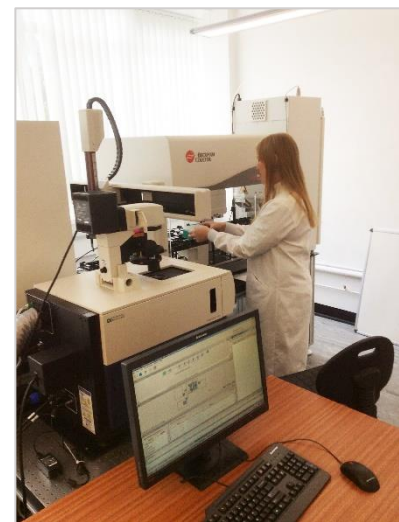
- *Fasciola hepatica* and *Fasciola gigantica* – parasitic trematodes with global impacts on the food and livestock production industry.¹
- Rising resistance to main flukicide, triclabendazole.¹
- Histone modification enzymes (HMEs) are targets of anti-cancer treatments due to involvement in transcription control.²
 - Could existing HME inhibitors be repositioned as flukicides, saving time and money?
- Evidence of phenotype and survivability effects of HME inhibition in *Schistosoma mansoni*, a close relative of *F. hepatica*.³
 - Previous Aberystwyth-based research project demonstrate encouraging results in *S. mansoni* HMEi development.⁴

Project Roadmap

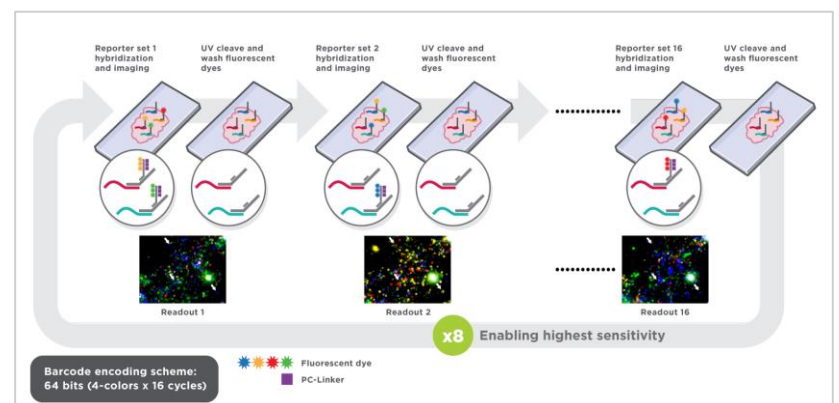


Planned Work – Technology at Aber

- High-throughput compound screening – RoboWorm platform allows automated imaging/video capture (right).
- Motility and phenotype scoring of newly excysted juvenile *F. hepatica*.
- Targeted transcript expression and localisation using multi-omics NanoString platform (below).
- Development of AI-based imaging platform following earlier work in *S. mansoni* – collaboration with Informatics Unlimited (Cambridge).



Life Science Research Network Wales (2013) <https://www.lsrnw.ac.uk/platform-technologies/roboworm-increasing-the-speed-of-anthelmintic-drug-discovery/>



NanoString (2021) <https://www.nanostring.com/products/spatial-molecular-imaging/spatial-molecular-imaging-technology-overview/>

References.

- ¹ Beesley *et al.*, (2017) *Int. J. Parasitol.*, 47(1), 11 – 20.
- ² Biancotto *et al.*, (2010) *Adv. Genet.*, 70, 341 – 386.
- ³ Pierce *et al.*, (2012) *Curr. Pharm. Des.*, 18(24), 3567 – 3578.
- ⁴ Padalino *et al.*, (2018) *Int. J. Parasitol.*, 8(3), 559 – 570.