

Master's Thesis

Drug Discovery for Neglected Tropical Helminth Infections

Helminth Drug Development Unit, Swiss Tropical and Public Health Institute

Soil-transmitted helminthiasis (STH) belongs to neglected tropical diseases that is widely distributed in tropical and subtropical areas. STH affects hundreds of million people worldwide causing a major public health burden. Treatment and control relies on a few drugs that are abundantly used in preventive chemotherapy campaigns. Considering the threat of emerging drug resistance, there is a need to identify and develop novel treatment options.

This master projects aims at enabling the discovery of effective combinations with emodepside (currently in phase 2 clinical trials against STH) targeting helminth larval and adult stages of different species. Most promising combination candidates will be then tested in *in vivo* models to further characterize their effectivity portfolio.

The MSc candidate will be guided through the early drug discovery process and learn new tools and techniques to:

- conduct primary and secondary screenings and evaluate the combination activity profile in larva and adult worms
- select the most promising combination/s and visualise its effect/s on parasites larva and adult worms under the fluorescence microscope.
- conduct CYP-450 metabolic drug-drug interaction studies

By the end of the project the MSc candidate will have gained insights into drug discovery for neglected parasitic diseases in addition to a detailed knowledge of parasite biology, including parasite culture, small molecule handling, data analysis and presentation skills. For further reading / references see:

Karpstein, Tanja et al. "Evaluation of emodepside in laboratory models of human intestinal nematode and schistosome infections." *Parasites & vectors* vol. 12,1 226. 14 May. 2019, doi:10.1186/s13071-019-3476-x

Mrimi, Emmanuel C et al. "Emodepside for *Trichuris trichiura* and Hookworm Infection." *The New England journal of medicine* vol. 388,20 (2023): 1863-1875. doi:10.1056/NEJMoa2212825

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