ROSkillers

Project partners
Université de Strasbourg, Université de Haute-Alsace, Universität Basel
Project duration / Awarded funding
01/02/2021 – 31/01/2023 / 48,000€
Short description of the project
The aim of this project was to identify protein targets of the antimalarial lead plasmodione in living cells/parasites, which could lead to the development of a more effective drug analogue against malaria parasites. In parallel, a library of newly synthetized diverse 3-benzylmenadiones was evaluated for antiparasitic activity/toxicity profile in order to select the most potent lead agents against parasites causing two neglected parasitic diseases (Chagas' disease & schistosomiasis) and to take them to preclinical studies.
Concrete implementation of the project (What was the funding used for?) (max. 500 characters (including spaces))
• we hired a post-doctoral biochemist with an experience in proteomics at LIMA-Strasbourg for 8 months. • We paid the conference fees for the postdoc to attend the 3rd PSL Chemical Biology Symposium (on-line), Paris, Jan. 12th - 13th, 2023. • Drug screenings were continuously performed in three parasite assays during the 2 years-long project at the STPH institute. • We organised a closure meeting at the STPH in Basel (January 25-26, 2023) with partners of Strasbourg University and Basel University.
Project result(s) and continuation of collaboration (max. 500 characters (including spaces))
• The proteomic and bioinformatics analysis of yeast and *E. coli* proteomes identified differently expressed proteins between WT and mutants of protein targets, • Drug screening of 200 new bMDs were performed in antiparasitic and cytotoxicity tests with *P. falciparum*, *T. cruzi*, and *S. mansoni*, rat L6 cells, respectively. • Optimized bMD analogues were selected: for *in vivo* testing in *P. berghei*-infected mice, as a new anti-Chagas early lead, or with potent antischistosomal activities.
Further information (links, articles, photos)
4 posters were presented by Ilaria Iacobucci or the partners from Strasbourg University: A4. Iacobucci I., Monaco V., Hovasse A., Schaeffer C., Blandin S., Cianferani S., Elhabiri M., Davioud-Charvet E. Activity-based Protein Profiling to investigate the interactome of the

antimalarial early lead Plasmodione. BSPR/EuPA 2023 Conference, Newcastle, July 17-20, 2023.

A3. Iacobucci I., Hovasse A., Schaeffer-Reiss C., Blandin S., Cianferani S., Elhabiri M., Davioud-Charvet E. Photoactivation of (pro-)activity-based proteome profiling probes to investigate the interactome of the antimalarial drug plasmodione. 3rd Joint Meeting of Spanish, French, and Portuguese Proteomics Societies (ProteoAix), June 20-23, 2023, Aix en Provence (France).

A2. Iacobucci I., Hovasse A., Schaeffer-Reiss C., Blandin S., Cianferani S., Elhabiri M., Davioud-Charvet E. Photoactivation of (pro-)activity-based proteome profiling probes to investigate the interactome of the antimalarial drug plasmodione. 3èmes Journées du GDR ChemBio, 8-9 juin 2023 Strasbourg.

A1. Iacobucci I., Hovasse A., Schaeffer-Reiss C., Blandin S., Cianferani S., Elhabiri M., Davioud-Charvet E. Photoctivation of (pro-)Activity-Based Proteome Profiling Probes to Investigate the Interactome of the Antimalarial Drug Plasmodione (UV-plasmoClick). MITI CNRS, Journée de Restitution des projets « Vie et Lumière », February 14, 2023, Paris.

One patent (optimized antimalarial drugs) is being submitted to CNRS$_{innovation}$ and five publications are in preparation:

three in the malaria project, one in the Chagas's disease project, one in the schistosomiasis project, at least, with co-authorships of partners of the EUCOR project.

An **ANR PRCI grant with the Swiss FNS** was granted **in 2022** (48 months) with 672.5 k€ for the French partners (3 teams: E. Davioud-Charvet, coordinator for France) and 581 kCHF for the Swiss partners (2 teams: Pascal Mäser (coordinator for Switzerland) et Jennifer Keiser (STPH)) to exploit the innovative 3-benzylmenadiones and their modes of action in the three parasites: *P. falciparum, T. cruzi, and S. mansoni*. The project is entitled: « Des benzylmenadiones redox-actives contre les parasites du paludisme et de la schistosomiase » (acronym: ROSaction), with a budget of 269 k€ for UMR 7042 CNRS – LIMA team), 270 k€ for Inserm U1257 (Stéphanie Blandin), 133 k€ for I2BC team (Brigitte Meunier). Link: https://anr.fr/Projet-ANR-22-CE93-0005