STSM grantee (1st period): Gülşah Bayraktar

Project Title: Design, Synthesis and Biological Evaluation of Antileishmanial Azaheterocyclic Compounds as Inhibitors of the Parasitic Exokinase CK1 (casein kinase 1)

Start and end date: 09/06/2023 to 17/07/2023

Home institution: Ege University

Host institution: Nantes University (Prof. Pascal Marchand)

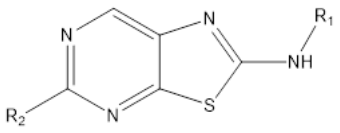
Leishmaniasis, a neglected tropical disease, is caused by a protozoa parasite from Leishmania species and it is transmitted to humans by the bite of the infected female phlebotomine sandflies. The drugs used for the treatment of Leishmaniasis are limited due to their side effects. Therefore, the development of a new generation of more effective and safer antileishmanials with a new mechanism of action to limit the devastating impact of parasite resistance are highly needed.

IICiMed team (hosting lab) and Institut Pasteur had selected and validated Leishmania casein Kinase I paralog 2 (L-CK1.2) as a drug target previously. L-CK1.2 is essential for intracellular parasite survival and released in macrophages via extracellular vesicles. Consequently, Casein kinase 1 (CK1) enzyme emerges as an important molecular target to tackle the disease.

Previously, a set of 10 thiazolopyrimidines already synthesized in the applicant's lab was received at the host's lab to test their antileishmanial activity on Leishmania donovani and L. major strains to complete the biological profile determined in Ege University. Considering both groups expertise, thiazolopyrimidine scaffold was selected and planned to be substituted with promising groups that IICiMed team recommended to obtain antileishmanial effect through the inhibition of L-CK1.2. The target compound was synthesized during STSM period and the purification process for the bioactivity studies that will carried out by the French group, will be continued at the applicant's lab.

Apart from these, the applicant has presented her work realised in Turkey during the group meeting of IICiMed team. The presentation followed by an extensive discussion with the multidisciplinary team members and formed novel ideas for the further collaborations.

Taken together, with this STSM, the first example of compound series that would merge two groups' expertise in the field to develop novel potential antileishmanial compounds was realized.



Designed title compounds