Dissecting the role of lipocalin in *Plasmodium falciparum*

Vitória Baptista[1,2,3,4], Miguel Silva[3,4], Susana O. Catarino[1,2] and Maria Isabel Veiga[3,4]

[1]Microelectromechanical Systems Research Unit (CMEMS-UMinho), School of Engineering, University of Minho, Campus de Azurém, Guimarães, Portugal

[2]LABBELS – Associate Laboratory, Braga, Guimarães, Portugal

[3]Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Campus de Gualtar, Braga, Portugal

[4]ICVS/3B's – PT Government Associate Laboratory, Braga/ Guimarães, Portugal

Malaria, caused by *Plasmodium* parasites, is an infectious disease responsible for millions of cases and deaths yearly. Despite the efforts, the disease control has been continuedly threatened by the resilient capacity of the parasite to acquire resistance to antimalarial drugs treatment, which target the symptomatic intraerythrocytic developmental cycle. During this cycle, *Plasmodium falciparum* uptakes hemoglobin from the host cell as a source of nutrients and to free space for growth. Hemoglobin digestion happens in the parasite's acidic food vacuole, where the resultant heme pool is detoxified through biomineralization into hemozoin. However, the mechanism of hemozoin synthesis is still unresolved. The area is highly controversial, with various compounds proposed to catalyze hemozoin formation. Theories include membrane lipids, histidine-rich proteins, the heme detoxification protein and, recently, the transport protein lipocalin, involved in the motion and morphology of the hemozoin crystals. Taking advantage of the advances in gene-editing and functional studies, we targeted the *P. falciparum* lipocalin, aiming to identify its role in hemozoin synthesis pathway, as well as its interactome. This work contributes to a better understanding of the underlying process that being vital and unique by the parasite is the prime target of most present antimalarial drugs. Furthermore, it uncovers novel players into this pathway, which remains a suitable target for next-generation antimalarial drugs.

This work was supported by NORTE-01-0145- FEDER-028178 funded by NORTE 2020 Portugal Regional Operational Program under PORTUGAL 2020 Partnership Agreement through the European Regional Development Fund and the by Fundação para a Ciência e Tecnologia (FCT). V Baptista thanks FCT for the SFRH/BD/145427/2019 grant. MI Veiga and S Catarino thank FCT for their contract funding provided through 2020.03113.CEECIND and 2020.00215.CEECIND, respectively.