

Hemozoin: the future in malaria diagnosis

Vitória Baptista^{1,2,3}, Carla Calçada^{1,2,4}, Miguel Silva^{1,2}, Miguel Teixeira^{1,2}, Pedro Ferreira^{1,2}, Graça Minas³, Weng Kung Peng^{5*}, Susana O. Catarino^{3*}, Maria Isabel Veiga^{1,2*}

1- Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Campus Gualtar, 4710-057 Braga, Portugal

2- ICVS/3B's - PT Government Associate Laboratory, Braga/Guimarães, Portugal

3- Microelectromechanical Systems Research Unit (CMEMS-UMinho), University of Minho, 4800-058 Guimarães, Portugal

4- Center for Neuroscience and Cell Biology (CNC), University of Coimbra, Coimbra, Portugal

5- Precision Medicine-Engineering Group, Department of Nanoelectronics Engineering, International Iberian Nanotechnology Laboratory, 4715-330 -Braga, Portugal

*- shared authorship

Prompt and accurate malaria diagnosis, both in symptomatic and asymptomatic individuals, is crucial for the disease control and elimination. Microscopy and/or immune-rapid diagnostic tests for long have been the standard diagnosis, nevertheless their limited sensitivity fails to detect low density infections. Detecting and treating these infections are of utmost importance to ensure patient health and to block disease transmission, since they are a reservoir for future infections.

As the disease proliferates, parasites infect red blood cells (RBCs), leading to biochemical and morphological changes. Malaria parasites digest host haemoglobin (Hb), releasing a toxic haem that is polymerized by the parasite into an inert crystal called the hemozoin (Hz). Parasite's survival relies on Hz formation, being this a unique biomarker of malaria's infection. Indeed, Hz has been exploited for malaria diagnosis in several ways. Hz formation induces transformation in the redox state of RBCs, increasing the bulk magnetic susceptibility of the infected RBCs (iRBCs). In the presence of an externally applied magnetic field, iRBCs present a considerable change in the transverse relaxation time (T_2) relative to non-infected RBC by nuclear magnetic resonance (NMR) system. In addition to its paramagnetic properties, the unique optical properties of Hz have also been explored. Considering that the Hz and Hb molar extinction coefficients differ significantly, especially at certain wavelengths, and their proportion is inversely related upon parasite maturation inside the RBC, each stage of malaria is characterized by specific absorbance and reflectance spectra, according to the Hb/Hz concentrations on the iRBC. Thus, herein, we focus on the detection of Hz for the development of an innovative non-invasive diagnostic device based on optical properties and on the detection and characterization of Hz along the parasites' life cycle using T_1 - T_2 correlational spectroscopy with a point-of-care NMR system. Both approaches led to promising results, suggesting us to be one step closer of a dream malaria diagnostic device.

Work supported by project NORTE-01-0145-FEDER-028178, funded by NORTE 2020 Portugal Regional Operational Programme, under the PORTUGAL 2020 Partnership Agreement, through the European Regional Development Fund and by Fundação para a Ciência e Tecnologia (FCT).