Implementing user-friendly electrochemical nanobiosensors to improve the management of malaria

Claudio Parolo^{1,2}, Ciara O'Sullivan^{1,3}, Jose Muñoz² ¹ INTERFIBIO Research Group, Departament d'Enginyeria Química, Universitat Rovira i Virgili, 43007 Tarragona, Spain ² ISGlobal, Hospital Clínic - Universitat de Barcelona, Barcelona, Spain ³ Institució Catalana de Recerca i Estudis Avancats (ICREA), 08010 Barcelona, Spain

claudio.parolo@urv.cat

Malaria is one of the most widespread parasitic diseases and ranks among the top three deadliest infectious diseases globally, alongside HIV and tuberculosis. This ranking is due to its high mortality rate and broad prevalence. In 2022 alone, malaria claimed over 600,000 lives, predominantly affecting children, pregnant women, and populations in nonendemic areas. Despite significant reductions in malaria cases due to aggressive public health initiatives and the advent of new vaccines, malaria continues to be a leading cause of death worldwide. This ongoing threat underscores the World Health Organization's emphasis on developing reliable point-of-care (PoC) diagnostic tests, which are crucial for guiding clinical decisions and assessing the impact of epidemiological interventions.[1]

Current diagnostic methods for malaria rely primarily on microscopic techniques and polymerase chain reaction. Although these methods are sensitive and specific, they are impractical for widespread screening due to their dependence on specialized personnel and equipment. Lateral flow assays (LFAs) have become the preferred diagnostic tools in low- and middle-income countries thanks to their affordability and ease of use. However, despite offering clinical sensitivities and specificities above 95%, the performance of LFAs has been compromised by the loss of the histidine-rich protein-2 (HRP2) antigen. leading to increased falsenegative results, especially in cases of Plasmodium falciparum infection. To mitigate this issue, some LFAs now include additional biomarkers, such as lactate dehydrogenase (LDH). Nonetheless, LFAs still suffer from significant drawbacks, including subjective result interpretation and a lack of quantitative output, which hinders their ability to assess disease severity. This highlights the pressing need for innovative biosensors that can provide rapid, reliable, and quantitative diagnostics to enhance malaria management, prognosis, and the allocation of healthcare resources.[2]

Electrochemical nanobiosensors, particularly aptamer-based electrochemical sensors, are becoming increasingly recognized as viable solutions for diagnosing diseases in settings with limited resources. These sensors are user-friendly, cost-effective, and robust, making them ideal for widespread deployment. They function by detecting binding-induced conformational changes in the aptamer upon encountering a target molecule, which then generates a quantifiable electrochemical signal.[3] This innovative mechanism enables rapid, sensitive, and precise analysis, thus empowering healthcare workers to make well-informed decisions directly at the point of care. A key advantage of these sensors is their capability to accurately quantify both parasite and host biomarkers. The levels of these biomarkers can be directly correlated with the severity of the disease, enabling healthcare providers to effectively triage patients based on the risk of developing severe symptoms.

In this presentation, we will first address the unique challenges associated with diagnosing malaria and, crucially, providing timely prognosis. We will then explore a range of available nanobiosensing designed technologies to overcome these challenges, with a specific focus on a recently developed electrochemical aptamer-based sensor that facilitates the quantification of the malaria biomarker LDH (Figure 1). Furthermore, we will discuss the future steps necessary for implementing these sensors into low-cost, graphene-based portable electrodes,[4] potentially transforming malaria diagnostics and contributing significantly to global health efforts.

References

- [1] W. Health Organization, World Malaria Report 2020: 20 Years of Global Progress and Challenges, 2020.
- [2] World Malaria Report 2023, Geneve, 2023.
- [3] C. Parolo, A. Idili, J. Heikenfeld, K.W. Plaxco, Lab Chip 23 (2023) 1339–1348.
- [4] L. Baptista-Pires, C.C. Mayorga-Martínez, M. Medina-Sánchez, H. Montón, A. Merkoçi, ACS Nano 10 (2016) 853–860.

Figure



Figure 1. The detection of the malaria biomarker LDH may allow the prompt diagnosis and timely prognosis of malaria at the point of care.