Development of a rapid diagnostic test for diagnostic and prognostic of malaria

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Introduction. Malaria is the leading cause of fever in international travelers and in the 2-23% of the cases produces severe symptoms (including death)[1]. Although appropriate treatment can almost entirely reduce mortality, current methods for prognosing malaria, which assess the risk of developing severe symptoms, are not reliable. A tool able to precisely prognose malaria during the initial visit would allow for a better patient management. In order to provide a solution for this need, we developed a lateral flow assay (LFA) for the detection of two prognostic biomarkers: angiopoietin-1 (ANG1) and angiopoietin-2 (ANG2)[2].
Methods. First, in order to identify the cut-off levels of host biomarkers (ANG1, ANG2 and sTREM) associated with severity[2], we analyzed a retrospective cohort of 132 patient samples using commercially available ELISA kits. Then, following a recently published protocol[3], we developed a LFA using gold nanoparticles for the detection of ANG2 and ANG1, whose ratio provided the best prognostic performance. To optimize the assay, we tested 12 different antibodies, 3 nitrocellulose membranes, 3 running buffers, and their specificity.
Results. From the analysis of the biomarker levels, the ANG2/ANG1 ratio provides the best performance with an area under the ROC of 0.82, which is similar to the values obtained by the current gold-standard methods. The measurements of the developed LFA was able to detect concentrations of ANG1 between 50 ng/ml to 1000 ng/mL and of ANG2 between 40 ng/ml and 1000 ng/ml[4], concentrations respectively within the clinical relevant range of ANG1 (5-200 ng/mL) and just above the one of ANG2 (2-15 ng/mL). The results confirmed that the developed LFA is specific for both targets. The use of the ImageJ software was feasible for the quantification of the biomarker concentrations.
Conclusions. We believe that developing and implementing more point-of-care prognostic devices is essential to shift from the common 'one-size-fits-all' approach to precision medicine, which allows for personalized patient management and optimizes available healthcare resources.

References

[1] World Health Organization, World malaria report 2020, (2020)
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[3] C. Parolo *et al.*, *Nature Protocols*, vol. 15, no. 12., pp. 3788–3816, (2020)
[4] A. Sena-Torralba *et al.*, *Adv. Mater. Technol.*, vol. 7, no. 8, p. 2101450, (2022)

Figures

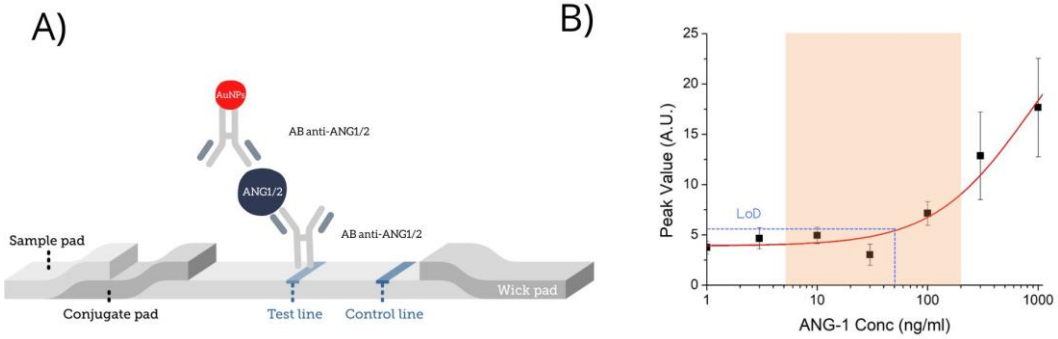

Figure 1: A) Representation of the main components and operation of a LFA schematic of the procedure based on immunosandwich recognition, with a positive sample testing B) Final prototype results with their limit of detection and the clinical range of ANG-1 Ab4/Ab7.