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Rapid single-molecule detection of COVID-19 and MERS antigens via nanobody-functionalized organic electrochemical transistors

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The COVID-19 pandemic has highlighted the need for rapid and sensitive protein detection and quantification in simple and robust formats for widespread point-of-care applications. We here introduce a modular nanobody-functionalized organic electrochemical transistors (OECT) architecture that enables rapid quantification of single-molecule-to-nanomolar levels of specific antigens in complex bodily fluids. The sensors combine a new solution-processable organic semiconductor material in the transistor channel and the high-density and orientation-controlled bioconjugation of nanobody–SpyCatcher fusion proteins on disposable gate electrodes. They provide results after 10-min of exposure to 5 μL of unprocessed samples, maintain high specificity and single-molecule sensitivity in human saliva and serum, and can be reprogrammed to detect any protein antigen for which nanobodies exist. We demonstrate the use of this highly modular platform to detect green fluorescent protein (GFP), SARS-CoV-2 and MERS-CoV spike proteins, and for the COVID-19 screening of unprocessed clinical nasopharyngeal swab and saliva samples with a wide range of viral loads.

References

[1] **Guo, Keying**, et al. Rapid single-molecule detection of COVID-19 and MERS antigens via nanobody-functionalized organic electrochemical transistors. *Nature Biomedical Engineering*, 5, 666–677 (2021)