Rapid single-molecule detection of SARS-CoV-2 with a bioelectronic sensor

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Background

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. What has remained elusive so far are methods that detect proteins rapidly and from unprocessed samples while, at the same time, reaching sensitivities that are comparable to the more complex laboratory methods such as PCR.

Methods

We have constructed nanobody-functionalised organic electrochemical transistors with a modular architecture for the rapid quantification of single-molecule-to-nanomolar levels of specific antigens in complex bodily fluids. The sensors combine a solution-processable conjugated polymer in the transistor channel and the high-density and orientation-controlled bioconjugation of nanobody–SpyCatcher fusion proteins on disposable gate electrodes.

Results

Our sensors 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 if a corresponding specific nanobody is available. We used the sensors to detect green fluorescent protein, 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.

Conclusion

The speed, performance and versatility of our nanobody functionalised OECT, and its compatibility with many sample types, suggest that this biosensor technology can complement or replace a wide range of clinical and non-clinical diagnostic assays.

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References

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