MAY 06, 2020
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BIOSENSORS FOR PANDEMICS

"A rapid and sensitive bioelectrical biosensor for the detection of the SARS-CoV-2 S1 spike protein based on membrane-engineered cells"

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ABSTRACT

As a result of the COVID-19 pandemic, novel diagnostic tools are needed to reliably monitor of infected individuals, particularly including asymptomatic patients and/or during the first days following of infection. Therefore, we developed a novel biosensor for the SARS-CoV-2 S1 spike protein antigen. The biosensor was based on measuring changes in the bioelectric responses of membrane-engineered mammalian Vero cells bearing the human chimeric spike S1 antibody, according to the principles of the Bioelectric Recognition Assay [1] and the technology of Molecular Identification through Membrane Engineering [2]. The biosensor was able to detect the viral antigen in three minutes without any prior sample processing and with a high sensitivity (fg/mL level) and selectivity against other virus-associated proteins. In addition, we have coupled our approach with a Point-of-Care recording device which can be operated by lay users with minimum training via a smartphone.

BIOSENSOR ASSEMBLY

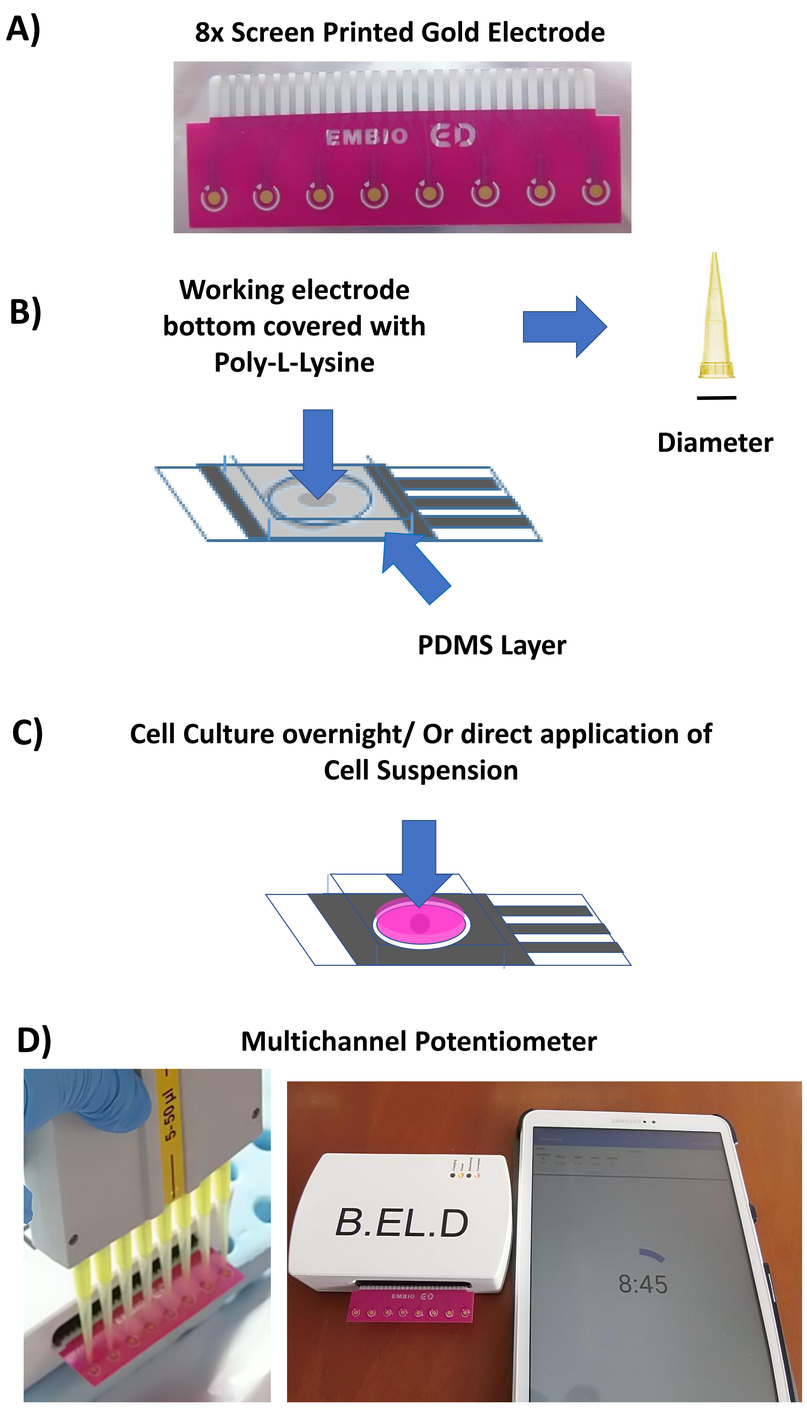

Figure 1: Presentation of the process for developing a Bioelectic Recognition Assay for the detection of the SARS-CoV-2 S1 spike protein antigen using membrane-engineered cells as biorecognition elements.

BIOSENSOR ASSAY PRINCIPLE

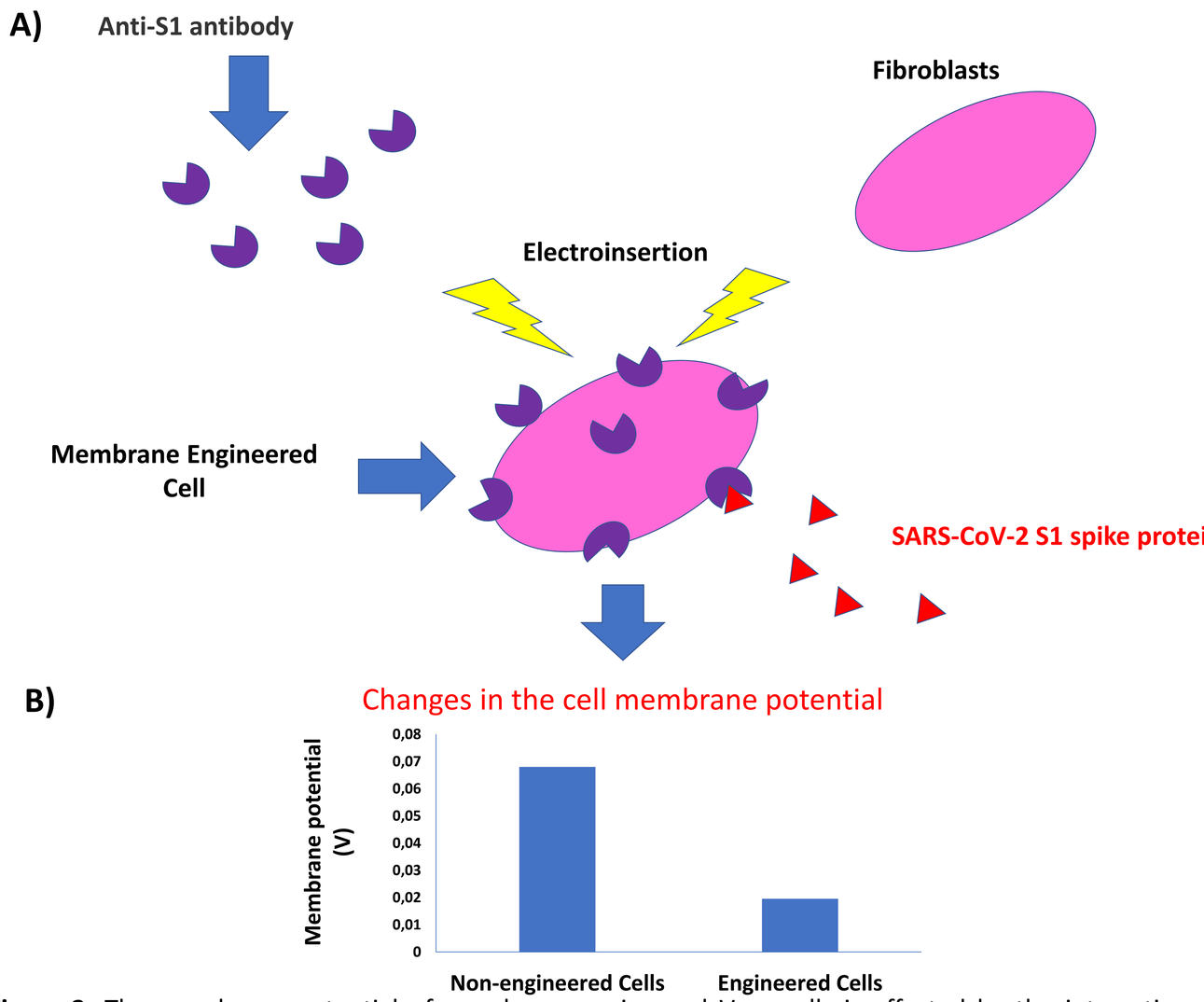

Figure 2: The membrane potential of membrane-engineered Vero cells is affected by the interactions of electroinserted receptor molecules and the analyte anions, producing measurable changes in the membrane potential.

BIOSENSOR DEPENDENT RESPONSE ON THE CONCENTRATION OF THE SARS-COV-2 SPIKE S1 PROTEIN

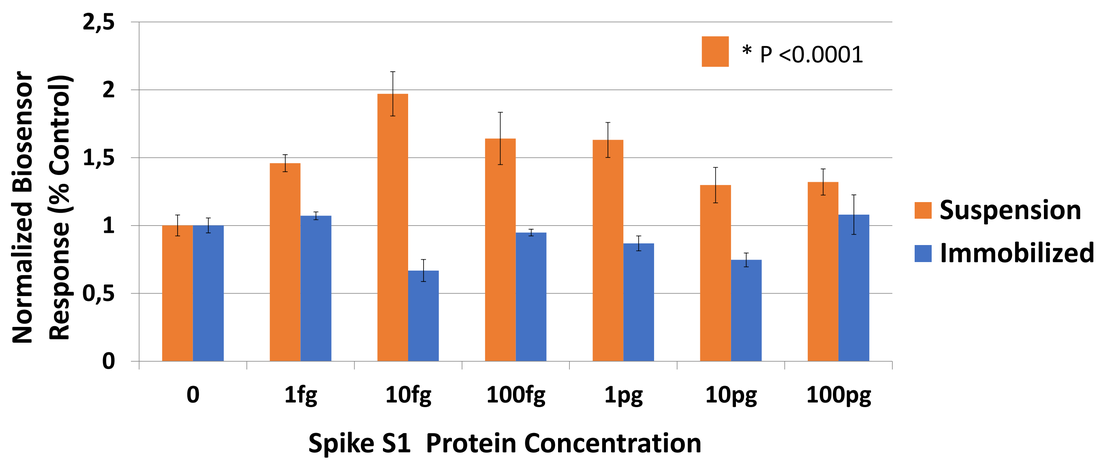

Figure 3: Concentration-dependent biosensor responses against the SARS-CoV-2 spike S1 protein. Vero/anti-S1 cells membrane-engineered with 0.5 μg/mL human chimeric antibodies were used as the biorecognition element. Results are presented as a normalized response of the control of a 3 min measurement. Red columns) depict the results of suspension cultures whereas blue columns depict the responses of adherent cells cultured on the working electrode's surface. *: statistically significant different results ($p < 0.0001$). Results are expressed as normalized biosensor responses (% control).

CONCLUSIONS

- Proof of the methodological concept of the novel biosensor assay for the detection of the SARS CoV-2 spike S1 protein.
- Next step = clinical validation of the assay using patient samples and compared to current serological and molecular tests.
- Assay optimization by expanding the number of cell lines to be membrane-engineered with the human chimeric spike S1 antibody and by further investigating the cross-reactivity and specificity of the biosensor.
- Improvement of the interface of the read-out device with an embedded software able to present to the end user with final results as a functional decision-support tool.

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[2] Kokla A, Blouchos P., Livaniou E., Zikos C., Kakabakos S.E., Petrou P.S., Kintzios, S., Visualization of the membrane-engineering concept: evidence for the specific orientation of electroinserted antibodies and selective binding of target analytes, Journal of Molecular Recognition 26, (2013), 627-232.

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