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EXPANDING THE CAPABILITIES OF WASH-FREE, ELECTROCHEMICAL DNA SWITCHES FOR THE DETECTION OF DIAGNOSTIC ANTIBODIES IN AUTHENTIC HUMAN SAMPLES

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A fast and precise diagnosis of infectious diseases -and thus the initiation of their treatment- is paramount to achieve a positive course of the disease. Here we present a novel wash-free, electrochemical sensor that measures the levels of specific antibodies directly at the point-of-care and during the few minute timeframe of a typical doctor´s appointment.
Our platform, named E-DNA sensors, consists of a short, double-stranded nucleic acid attached by one end via a flexible linker to a gold electrode and modified on the other with a redox reporter (methylene blue) and an epitope/antigen (Fig.1-A). The binding of the specific antibody reduces the rate of electron transfer from the methylene blue to the electrode, generating a measurable change in the electrochemical signal, which we use to quantify the target concentration. E-DNA sensors are reagentless, single-step, and selective enough to deploy in whole blood serum, making them excellent candidates for point-of-care applications. In addition, the equilibration time constant of antibodies, generally in the order of few minutes, matches our “timeframe-goal”.
We demonstrated that we can include as recognition elements of our sensing platform not only linear epitopes but also full-size antigens (<70 kDa, Fig.1-B). Taking advantage of this modularity, we designed five sensors employing different epitopes from the HIV-antigen gp41 and one using the full p24 antigen. After confirming the immunogenicity of each epitope/antigen, we simultaneously detected multiple HIV-specific antibodies directly in human samples. We achieved the same clinical sensitivity and specificity as those of ELISAs and lateral flow immunoassays, being able not only to discriminate between healthy and HIV-positive patients, but also to differentiate early-infected from late-infected individuals (Fig.1-D).
The E-DNA platform appears a versatile, clinically sensitive and specific method for the rapid, single-step detection of antibodies at the point-of-care.

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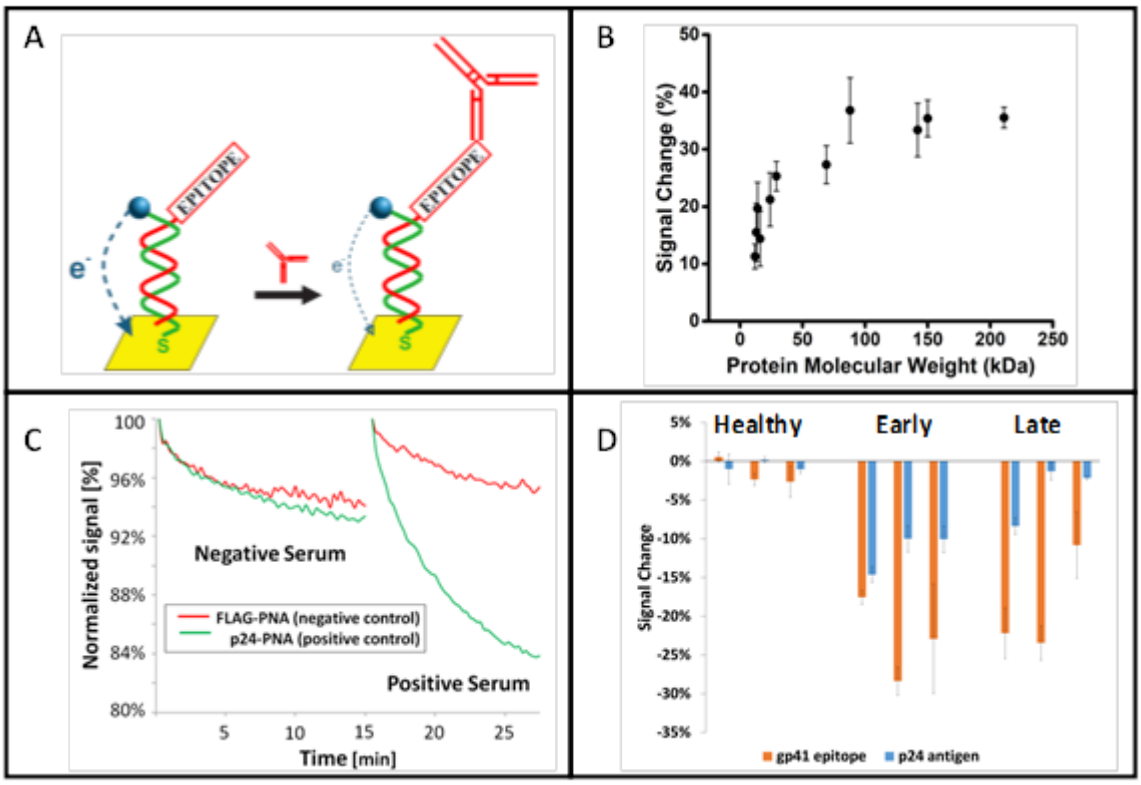

Figure 1. A) Cartoon of the E-DNA electrochemical antibody sensor. B) Impact of the antigen size on the binding-induced signal change. C) Continuous measurement of HIV-positive and HIV-negative serums using E-DNA sensors. D) Discrimination of healthy, early-infected and late-infected HIV-positive patients using E-DNA sensors.

References

[1] Kang D., Parolo C., Sun S., Ogden N. E., Dahlquist F. W., and Plaxco K. W., ACS sensors, 2018, 3, 7, 1271-1275