ers GENOMICS

CRISPR ON YOUR WRIST

Wearable CRISPR microneedle patch for extraction & monitoring of cell-free DNA.

Introduction

The field of wearable technology has witnessed remarkable advancements in recent years, particularly in the realm of personalized medicine. Wearable devices hold great potential for providing in-depth medical diagnostics and facilitating personal health assessments.
While most wearable technologies have focused on analyzing small molecules or electrolytes, the next generation of wearables aims to detect macromolecular biomarkers such as proteins or DNA. Extracting and monitoring these biomarkers in real-time pose significant challenges for wearable devices.

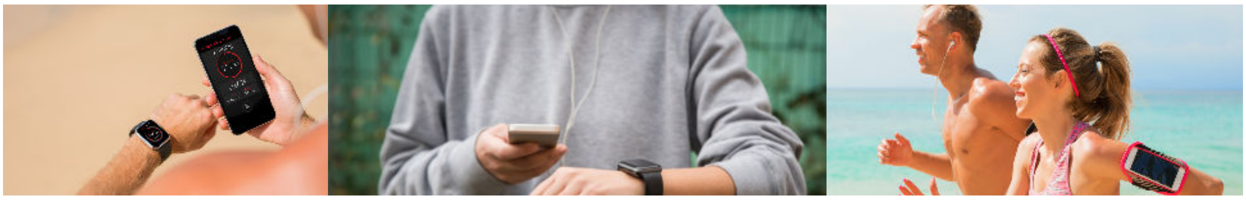
The interstitial fluid (ISF) has emerged as an ideal source for wearable chem-biosensors, as it contains various biomarkers closely related to blood concentration. Microneedles (MNs) are a key component of wearable devices for safe, painless, and efficient extraction of biomarkers from the ISF. Previous studies have proposed hydrogel MN patches for DNA extraction from the ISF, followed by offline analysis using portable electrochemical microfluidics. However, this approach is limited in its ability to perform real-time monitoring, hindering its potential integration into integrated wearable devices for real-world applications. The development of an online wearable system that can extract samples and perform real-time monitoring would greatly improve personal health management.

The emergence of clustered regularly interspaced short palindromic repeats (CRISPR) technology has redefined the field of nucleic acid analysis. CRISPR enables precise gene editing using programmable single guide RNA (sgRNA) or CRISPR RNA (CrRNA) and has been extensively employed for sequence-specific nucleic acid detection, offering highly specific and accurate analysis.

In a 2022 Nature paper, Yang, Kong & Fang designed a wearable patch that integrates CRISPR-activated graphene biointerfaces with microneedles for efficient extraction and real-time monitoring of cell-free DNA (cfDNA). The wearable system aims to monitor cfDNA associated with Epstein-Barr virus, sepsis, and kidney transplantation.

Is this some sort of CRISPR Apple Watch?

Sort of ...in some ways yes but in others this is on a different level. The online wearable patch developed in this study combines CRISPR/Cas9 technology with graphene biointerfaces to enable real-time monitoring of target cfDNA. The system comprises a modified polydimethylsiloxane (PDMS) membrane as a flexible substrate, a carbon nanotube (CNT)-functionalized component for target cfDNA enrichment control, and a three-electrode prototype CRISPR/Cas9 MN system for real-time monitoring control.



The modified PDMS membrane is treated with plasma to enhance hydrophilicity, and a hydrophilic membrane is created on its surface using chitosan solution. CNTs are then spray-printed onto the PDMS membrane, serving as a reverse iontophoresis compartment for separating negatively charged compounds, including nucleic acids. The CRISPR MN, acting as the working electrode, is attached to the anode side of the CNT pattern. The CRISPR MN performs three functions during real-time detection: (I) insertion into the epidermis for target DNA isolation and concentration, (II) CRISPR gene capture through Cas9/sgRNA immobilization on the MN surface, and (III) formation of a three-electrode system to record electrical signals.

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Patching you through to the future?

The proposed patch demonstrates high effectiveness in the extraction and real-time monitoring of target cfDNA. The CRISPR-Cas9 activated wearable patch enables continuous monitoring of cfDNA targets in vivo, with a detection limit of 1.2 fM for the CRISPR MN. The patch exhibits good electrochemical performance and stability for 10 days in vivo. The programmable dRNP within the wearable microneedles allows for the specific recognition of different target cfDNA. The authors suggest that this method can be applied to various genomic sites of a single target cfDNA.

The development of these wearable CRISPR patches holds significant implications for the future of healthcare and personalized medicine. Here are some potential applications and their implications:

-Early Disease Screening, Surveillance & Outbreak management:

The patch has the potential for early detection and screening of diseases by monitoring specific cfDNA biomarkers associated with various conditions and infectious disease. Potential identification of diseases at earliest stages, facilitating timely interventionsto track the spread of diseases, identify hotspots, and implement targeted interventions to control outbreaks.

-Prognosis and Disease Monitoring:

Real-time monitoring of cfDNA can provide valuable insights into disease progression and treatment response. The wearable patch could continuously monitor changes in cfDNA levels associated with specific diseases, allowing for personalized disease management and timely adjustments to treatment plans.

-Integrated Healthcare Systems:

Potential for integration into existing healthcare systems, allowing for seamless data collection and analysis. Healthcare professionals could access real-time data on cfDNA biomarkers remotely, enabling remote monitoring, personalized treatment adjustments, and improved patient care.

-Personalized Health Management:

Wearable devices equipped with real-time monitoring capabilities can empower individual ownership of health and wellness. By providing continuous feedback on biomarker levels, the wearable patch could support self-management and proactive healthcare decision-making.

Final remarks: Promises vs. Delivery

While the proposed system shows promise for disease monitoring, there are challenges that need to be addressed. The stability of the immobilized bioreceptor and the fluctuation of the interface between the device and the active sensitive film during dynamic deformation are critical issues. Additional measures, such as the use of hydrogel or chitosan layers, can protect the immobilized bioreceptor and mitigate these challenges. Sensitivity is another area for improvement, as the current version of the amplification-free strategy falls short in meeting the requirements of highly sensitive DNA detection.

Overall, the patch represents a significant advancement in wearable technology and personalized medicine. Its potential applications span early disease screening, personalized health management, disease monitoring, and research, holding great promise for improving patient care, enabling proactive healthcare interventions, and advancing our understanding of various diseases.

Yang, B., Kong, J. & Fang, X. Programmable CRISPR-Cas9 microneedle patch for long-term capture and real-time monitoring of universal cell-free DNA. Nat Commun 13, 3999 (2022). https://doi.org/10.1038/s41467-022-31740-3