AI-POWERED DIAGNOSTICS

A Closed-loop Wearable Platform For Synthetic Biology-powered Sensing And Delivery Of Interventions

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We present a novel platform that exploits synthetic biology for sensing biomarkers related to different conditions and delivery of biochemical interventions in a wearable patch format. This closed-loop system requires no user intervention to monitor and mitigate any issues that can be encountered in the field, including performance degradation due exposure to different chemical and biochemical threats. We have designed a polymeric microneedle patch that contains engineered bacteria and penetrates the skin, accessing the rich variety of biomarkers present in the dermal interstitial fluid (ISF). Importantly, this plaform takes advantage of decades of work in drug delivery through microneedles, providing a safe means to deliver biochemical interventions, facilitating transition to the field. Compartmentalization of the engineered microbes in a wearable device, instead of culturing the engineered bacteria directly in the skin microbiome, is designed to isolate the bacteria from the harsh environment of the skin (dryness, pH, etc.) which makes it challenging for organisms that are not part of the native skin to function in these conditions. Additionally, this approach prevents issues that may arise due to competition with other organisms present in the skin microbiome that could interfere with the engineered cell's function. To develop this sense/assess/intervene platform, we engineered E. coli Nissle 1917 with circuitry that exploits transcription factors as sensing elements to recognize cortisol in the ISF physiological range. Cortisol sensing was coupled to a synthetic pathway that activates production of serotonin, a mood regulator, and the materials formulation was optimized to maintain the cellular sentinel's performance when integrated in the polymer hydrogel. The system was tested in skin surrogates, demonstrating cortisol sensing-modulated serotonin release, realizing a closed-loop system. The same approach was utilized to develop a sensor for lactate, a biomarker for physical fitness and sepsis, covering the ISF biological range, showing the versatility of these technology. We propose that by exploiting the versatile toolset of synthetic biology to engineer different sensing mechanisms and potential interventions, including delivery of chemicals, miRNAs and gene editing tools to regulate gene expression in a controllable and personalized fashion, this platform can be leveraged as a fieldable solution to detect and treat exposures to bio- and chemical-threats.

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