

NSF 22-077

Dear Colleague Letter: Sentinel Systems that **D**etect, **Re**cognize, **A**ctuate, and **M**itigate Emergent Biological Threats **(DREAM Sentinels)**

April 26, 2022

Dear Colleagues:

As we approach the third year of the COVID-19 pandemic, we have learned a tremendous amount about the detection and evolution of coronaviruses and their reservoirs in the environment, yet we are still largely unprepared to quickly sense and respond to the next emergent biological threat prior to its evolution in its host or transmission to human populations. Thus, there is an urgent need for the creation and development of novel biotechnologies **for sensing and responding** to known and unknown biological threats. At the heart of any of these new biotechnologies will be flexible and potentially modular biosensing/actuating platforms capable of detecting and responding to emerging threats.

There have been tremendous advances in biotechnologies in the past several years, including the discovery and application of CRISPR-Cas systems for not only genome editing, but also for many different nucleic acid recognition applications. Such systems have the potential to achieve the combined tasks of recognition and transduction needed for highly specific sensing, actuation, and signaling on one platform. Advances in the integration of biological systems with semiconductors have enabled biological information read, write, store, and compute capabilities. New tools and technologies based on cellular and immune engineering, neural engineering, synthetic biology, protein engineering and design, in combination with AI and machine learning, are bringing new capabilities to bear on the detection of and response to emergent biological threats.

With this Dear Colleague Letter (DCL), we highlight the continued interest of existing programs in the Directorate for Engineering (ENG) and the Directorate for Biological Sciences (BIO) in interdisciplinary research for the creation and development of novel biosensing/actuating All-In-One platforms for rapidly evolving or emerging biological threats. This DCL includes the topical interests called out in **DCL: Sentinel Cells for the**

Surveillance and Response to Emergent Infectious Diseases (Sentinels) (NSF 20-105), Predictive Intelligence for Pandemic Prevention Phase I: Development Grants (PIPP Phase I) (NSF 21-590), and others.

All proposals submitted in response to this DCL should include biosensing and bioactuation elements that address a biological threat. The biosensing element should leverage the power of modern biotechnology and deliver robust and specific recognition of the biological threat. The results of bioactuation should alert the user, destroy the threat, protect the host, or initiate an immune response or other strategies that would mitigate the threat. Other possible areas of interest include but are not limited to:

- Novel tools or approaches that enable the prediction of the evolution of current biological threats and leverage the predictive power for the creation of platforms to detect emergent variants of existing threats.
- Modular technology designs that can easily be reprogrammed and deployed once a new threat is identified.
- Novel sensing modalities that are adaptable and/ or evolvable such that the hybrid sentinel systems are robust to a range of emergent threats, and/or can easily be reprogrammed and deployed once a new threat is identified.
- Sentinel systems that detect and respond to biological agents in a broad range of hosts that could serve as reservoirs for future pandemics.

Investigators are encouraged to think broadly about innovations leveraging biology and engineering to advance adaptable detection of emerging biological threats.

Proposals submitted in response to this DCL should have a title prefaced with "DREAM Sentinels:". Proposals should be submitted to one of the following programs:

- The Biosensing Program (PD 20-7909), a part of the Engineering Biology and Health Cluster in the Division of Chemical, Bioengineering and Environmental Transport Systems (CBET)/ENG
- The Systems and Synthetic Biology cluster, in the Division of Molecular and Cellular Biosciences (MCB)/BIO

Both the Biosensing Program and Systems and Synthetic Biology cluster accept proposals without deadline. Proposals are reviewed as they are received.

It is anticipated that up to \$3,000,000 will be allocated annually for DREAM Sentinels awards, subject to the availability of funds.

Points of Contact: Investigators interested in submitting a proposal are strongly encouraged to contact one of the Program Directors listed below for further information:

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Sincerely,

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