REVOLUTIONARY DIAGNOSTICS – NONTRADITIONAL APPROACHES FOR DEVELOPING BREAKTHROUGH CAPABILITIES AGAINST EMERGING THREATS

Development Of A Tunable Metal-organic Frameworks (mofs)-dna Sensor Platform For Rapid Viral Detection

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Rapid and sensitive viral detection is necessary to identify sick individuals in need of treatment and to limit the spread of infection. Viruses can spread rapidly from person to person as an individual may be unaware that they are infectious. To date, many methodologies for viral detection rely on amplification-based nucleic acid detection, for example qPCR, which, while highly specific and sensitive, is time consuming and requires specialized equipment and temperature-controlled reagents. This work focuses on the development of a modular metal-organic framework (MOF)-DNA sensor platform for specific viral detection. Recently, MOF-based detection has been demonstrated for a variety of viruses including HIV, Hepatitis B, Zika, Ebola and Dengue. Furthermore, multiplex detection of up to 3 targets has been demonstrated, with detection as rapid as 2 minutes. While MOF-based viral detection is theoretically amenable to detection of any viral sequence, the technology is currently nascent, and the MOF features necessary for sequence agnostic detection are currently unknown.

Here, we will present our recent work to understand the structure-function relationships between the MOF components and the DNA probes. To create the sensor system, the MOF must capture the oligo probe and quench the associated fluorophore. These steps are mediated by the linker and metal respectively. Following exposure to the target DNA or RNA, the probe releases from the MOF and the fluorescent signal is regained. To gain understanding of this system, we have created a library of MOFs with a variety of linkers and metals with both ideal and defective structures to explore the necessary structural features of the MOF for highly specific and sensitive viral detection. We have complemented this library with a series of different DNA oligo probes with varied sequence composition (GC and AT content) and length to determine the ideal features of the probe. Using this library, we have determined the effect of linker chemistry and metal selection on the efficiency of the interaction with the oligo probe, which determines the background signal and dynamic response range. We then determined the effect of MOF and probe selection on the sensitivity and specificity of target detection.

Our work provides a framework for the use of MOF-DNA sensors as a platform technology capable of rapid viral detection with minimal equipment. As a platform technology, the MOF-DNA sensor can be adapted to rapid detection of new and emerging viruses based on our predetermined design characteristics.

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