MITIGATION - SCIENCE AND TECHNOLOGY ADVANCES FOR CHEMICAL AND BIOLOGICAL HAZARD MITIGATION

Towards The Agnostic Future Of Diagnostics: Untargeted Nanopore Sequencing Of Biological Fluids

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Current methods for diagnosis of bacterial and viral infections include cultivation of microorganisms, identification of antigens, detection of antibodies, and detection of nucleic acids. These are all targeted approaches and new assays must be developed and implemented for new threats in lengthy development and approval processes. Therefore, development of agnostic platforms will be crucial to avoid delays in diagnostics, treatment, and development of countermeasures. Nanopore sequencing technologies are quickly evolving and provide low-cost, portable, easy-to-set up devices to rapidly detect biological threats without the limitations of targeted approaches or target panels. Long reads and live base calling coupled with appropriate bioinformatics tools allows entire genomes to be analyzed even in complex sample matrices for detection, even in the case of previously unknown human pathogens or engineered threats. Our overall scientific goal is to establish and validate sequencing protocols to detect human pathogens from biological fluids that are routinely used for disease diagnosis, can be easily collected by clinicians, and are minimally invasive: saliva, urine, and blood. A full process from sample collection, stabilization and storage, processing, untargeted nanopore sequencing, and bioinformatic methods will be developed for the identification of bacterial and viral pathogens from these biological fluids. Current work is focused on workflows towards untargeted identification of bloodborne pathogens. Successful methods to store samples (under different temperature conditions) and recover microbial nucleic acids are being earmarked. Sequencing conditions and bioinformatic pipelines are continuously being assessed and optimized to generate results that are clear and inspire confidence in making a timely diagnosis. Successful implementation of an untargeted nanopore sequencing system for diagnostics would enable rapid identification of any new, unknown, or engineered microorganism at even remote or low-resource sites of outbreaks to inform decision making.

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