Classification of anti-microbial resistant pathogens using solid-state nanopores

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According to a World Health Organization (WHO) report, antibiotic resistance is reaching dangerously high levels worldwide and is threatening our ability to treat common infections. Since this trend is accelerated by the overuse and misuse of antibiotics in clinical care, our approach is to develop an early and accurate method for the genotyping of pathogens targeting genetic features such as single nucleotide variations (SNVs), insertions and deletions. We develop a direct, solid-state Nanopore (ssNP) and ligation-based, genotyping technique that circumvents DNA amplification and sequencing, and uniquely transforms genetic variations to molecular-encoded barcodes. This allows for specific classification of the given bacterial genome. The DNA barcode formation method utilizes a sequence-specific ligation reaction using a set of probes designed to target specific sequences in the genome. Following a biotin bead separation step, the ssDNA ligation products are then hybridized to oligonucleotides to the characteristic barcode sequence and are analyzed using an electro-optical ssNP sensor. The nanopore interprets the barcode which allows for unique classification of the source genome with high diagnostic accuracy and high multiplexing ability. This nanopore/ligation method provides an ultra-fast, high specificity and high-sensitivity detection and classification of a large variety of pathogens in the same mixture.

References

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