Rapid and comprehensive diagnosis of pathogens and infectious diseases (Ramot)

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Technology

A novel approach for pathogen detection using short reads generated by deep sequencing of short-RNA extracts was developed. This three step approach includes: (i) alignment of the short reads against the human reference genome; (ii) subtraction and assembly of the remaining unmapped reads; and, (iii) categorization and identification of the pathogen infection based on nucleic acid databases.

The entire process should take less that 12 hours as compared to several days with current technologies.

The Need

Early and accurate detection of human pathogen infection is critical for treatment and therapeutics. Most pathogen detection methods (PCR amplification or microarrays) rely on prior exact sequence knowledge of the potential pathogen or the ability to cultivate it (microbial cultures) which is unreasonable in many cases. An alternative detection technique recently offered, which circumvents these limitations, is the sequencing of infected cells and comparing the sequences to a reference pathogen library for identification. Given the massive increase in nucleic acid sequence databases of all organisms, and the advancement in massive parallel sequencing technologies, sequencing pathogen-infected cells evolves as an increasingly prominent and logical alternative path for pathogen characterization. The major advantages of this approach are the unbiased detection of all known pathogens, overcoming the requirement for cultivation, the ability to recognize pathogens even at minute expression levels, and the rapid turn around and processing.

Due to the decrease in cost and increase in efficiency of deep sequencing platforms, we expect sequencing utilization in the field of pathogen detection and identification to increase. Our method proves to be a useful tool for both sample contamination detection and pathogen identification using a calculated and cost-effective sample preparation and an easily-implemented computational pipeline appropriate for all types of current sequencing platforms. We envision early and accurate detection of pathogen infection using short RNA reads to accelerate.

Potential Application

Rapid pathogen detection in hospitals includes detection of bacteria, viruses, fungi and parasites. Since in some settings, or with particular patients, these infections are life threatening the potential applications and clinical relevance is immense. For example, immuno-supressed bone marrow transplantation patients are constantly monitored for potential infections. Similarly neonatal wards are at a continuous risk of being infected and transmitted between the newborns.

Stage of Development

We have run our detection algorithm on a set of virus and bacteria infections in cells lines. We have tested our method on clinical samples derived from patients. We have tested several preparation protocols and 4 deep sequencing platforms. We have rewritten the algorithm to detect minute amounts of reads and to score them for advanced processing.

Patents

Granted

Supporting Publications

Isakov O, Modai S, Shomron N. Pathogen detection using short-RNA deep sequencing subtraction and assembly. Bioinformatics. 2011 Aug 1;27(15):2027-30.

Isakov O, Ronen R, Kovarsky J, Gabay A, Gan I, Modai S, Shomron N. Novel insight into the non-coding repertoire through deep sequencing analysis. Nucleic Acids Res. 2012 Jun;40(11):e86.

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