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Cell-free DNA Test to Monitor Urinary Tract Infections

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Technology description

The invention provides a method to detect cell-free DNA of bacteria and viruses in urine using single-stranded DNA library preparation techniques for amplification by unbiased next-generation sequencing (NGS).

Urinary tract infections (UTI) occur at a high rate among kidney transplant recipients. The incidence of bacterial UTI is at least 20% in the first three months and 50% in the first 36 months after kidney transplantation. Conventional tools to diagnose UTI are mainly culture-based tests. These tools do not allow for detection of viruses or organisms that are not cultivablein vitro.

Cornell inventors have developed a method that leverages the presence of a large amount of small fragment of cell-free DNA (cfDNA) in order to detect and monitor viral and bacterial infections using unbiased sequencing (NGS) at one time. cfDNA are nucleic acid fragments that are released in the bloodstream during apoptosis or necrosis. They offers a vast window toward a non-invasive, rapid, sensitive and accurate method of diagnosis and monitoring tools in cancer, infectious diseases, pregnancy, solid-organ transplantation, etc. Urine represents an ideal specimen for the analysis because the level of host cfDNA background in urine is smaller than in plasma — what should not limit sensitivity of the method to pathogen detection.

In the present method, libraries have been prepared from extracted DNA using a single-stranded adapter ligation (Fig.1). This enables robust sequence analyses of urinary cfDNA from just one ml of urine.

Figure 1: Sequencing via ligation of single-stranded DNA (ssDNA) adapters.

As a proof of concept, the team assayed urine samples collected from renal transplant recipients with clinically confirmed UTIs. Using the novel method, they were able to confirm the infections and identify co-infecting microbes. They were also able to determine the replication rate and growth dynamics of various bacterial strains without the need for an annotated genome, making possible prediction of the efficacy of antibacterial drug therapies.

Additional Information

Burnham P., et al. (2017). Structure and diversity of urinary cell-free DNA informative of host-pathogen interactions in human urinary tract infection. BioRxiv preprint .

Application area

Detection and monitoring of infections

Research tool to predict the efficacy of antibiotics.

Advantages

Enable detection of organisms that are not cultivablein vitro

Enable detection of viruses

Non-invasive sample extraction (Urine collection).

Institution

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