Docket #: S20-025

Rapid, simultaneous detection of multiple N-acetyltransferase gene polymorphisms and prediction of isoniazid metabolism to optimize treatment of tuberculosis

In nearly all current medical practice for treatment of infectious diseases, a single treatment dose is used for all patients. However, metabolism of drugs varies considerably between individuals, such that some individuals will have too high of drug levels—at risk of toxicity—while others at the same dose will have too low of drug levels and be at risk for treatment failure and drug-resistance. Inventors at Stanford developed a method that will inform the clinician about risks of toxicities and the appropriate dosing adjustments. In sum, this platform can inform what drug should be used, for what duration and at what dose, using a single patient sample.

The invention is a method for rapid detection of pharmacogenetic markers of antimicrobial metabolism and toxicity that will be performed concurrently with rapid detection of pathogens on the same sample. Clinical samples, such as blood, sputum and oral swab, typically have pathogen DNA as well as abundant human DNA present in them. This method uses molecular assays that target single nucleotide polymorphisms (SNPs) associated with drug metabolism and toxicity on a point-of-care testing platform. In a short time, this platform can report what pathogen is present, and what drug-metabolism markers are present in the patient.

Stage of Development
Proof of concept

Applications

- Detect tuberculosis and human gene polymorphisms
- Analyze drug metabolism and toxicity

Advantages

- Haplotype prediction algorithm markedly outperformed the existing state of the art algorithm by achieving 99.9% accuracy using only 5 SNPs.
- There are no existing methods for: point-of-care detection of pathogens and pharmacogenomic markers (human SNP variants) on the same sample and platform
- Non-invasive sampling from sputum
- Fully automated NAT2-PGx assay is easy to perform and could be utilized in settings with minimal laboratory infrastructure
- The test developed here uses only 100ul of whole blood. The assay can further be optimized to perform with lower volumes. In such case, a finger stick sample collection method could be used.

Publications

- Verma, R., Patil, S., Zhang, N., Moreira, F. M., Vitorio, M. T., Santos, A. D. S., ... & Andrews, J. R. (2021). " A rapid pharmacogenomic assay to detect NAT2 polymorphisms and guide isoniazid dosing for tuberculosis treatment". American Journal of Respiratory and Critical Care Medicine, 204(11), 1317-1326.

Patents

- Published Application: WO2021188834
- Published Application: 20230132088

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