Ultrasensitive Molecular Residue Disease Detection Enabled by Genome Wide Concatmer Error Correction

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Background & objectives

While different features of cell-free DNA (cfDNA) have been utilized for early cancer detection, somatic mutation has been shown to offer the highest specificity for ctDNA detection. The recent drop of sequencing cost makes it possible to track thousands of somatic variants from the cancer genomes as cancer markers in plasma, achieving high sensitivity for molecular residual disease detection. This approach, however, will be limited by errors introduced during library preparation and sequencing. Here, we describe AccuScan, a highly accurate and efficient whole genome sequencing technology that enables effective genome wide error suppression at single read level.

Methods

AccuScan combines rolling cycle amplification with concatemer based error correction to remove both polymerase errors and sequencing errors.

Results

We deploy this technology in whole genome sequencing of cfDNA and demonstrated >95% sensitivity at 10^{-5} variant allele frequency with a specificity of 98% in an analytical study using contrived samples.

Conclusion

AccuScan provides a high performance and scalable MRD solution that is tumor informed without personalized design.