Ultra-sensitive tumor-informed ctDNA assay predicts survival in advanced melanoma patients treated with immune checkpoint inhibition

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Highly sensitive ctDNA detection down to parts-per-million-resolution

We demonstrated a broad dynamic range of ctDNA detections, from ~100,000 PPM down to 2.3 PPM, with a median limit of detection (LOD) of 1.97 PPM (A). The high sensitivity of the assay was reflected in a significant number of positive detections at low PPM levels, with 28% (22/76) of positive detections occurring below 100 PPM and 24% (18/76) occurring below 50 PPM. We also observed strong concordance with imaging findings, with 100% of ctDNA detections presenting correlated findings via RECIST when confirmed presence of tumor even at the lowest PPM levels. Similarly, 100% (39/39 timepoints) of complete responses (CR) assessed via RECIST were ctDNA negative for all corresponding plasma timepoints (B, example patient time course and RECIST shown).

Conclusions
We demonstrate that low ctDNA levels are commonly observed, even in late stage disease, with positive ctDNA detections in this study occurring as low as 2.3 PPM. Detections down to low PPM levels correlate strongly with imaging and RECIST-derived classifications of response. Our results further suggest that without the ultra-sensitive ctDNA detection achieved using NeXT Personal, patient MIRD status would have been misclassified at a significant number of time points in this cohort. Sensitive detection of ctDNA down to these low levels is critical for accurate interpretation of patient outcomes, including overall survival. Additionally, we demonstrate the potential for future clinical use of a unique aspect of our tumor-informed MIRD platform which identifies and tracks clinically actionable variants arising or changing in response to therapeutic pressure. The results presented here suggest the importance of ultra-sensitive ctDNA-based therapy monitoring which will be further validated as we expand the patient set.

References: