Detecting and monitoring circulating tumour DNA in dried blood spots from metastatic cancer patients and xenograft mouse models

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Background & objectives

Proof-of-principle studies have shown that circulating tumour DNA (ctDNA) can be detected in minute volumes of blood, even dried blood spots (DBS) from cancer patients and pre-clinical models (Heider et al., 2020 & Sauer et al., 2022). Adopting DBS for ctDNA could further simplify blood collection and may support novel clinical trial designs to increase the real-world utility of liquid biopsies, including studies involving blood sampling in hard-to-reach and vulnerable populations at which traditional phlebotomy is not feasible.

Here, we aim to investigate the potential of DBS as a means to simplify and diversify both, clinical and translational applications of ctDNA-based liquid biopsies.

Methods

Serial finger-prick DBS (fpDBS) were collected from ten patients with metastatic oesophageal cancer to study ctDNA dynamics. Similarly, 50µL of tail-prick blood were sampled in serial time-points from three mouse tumour models: patient-derived ovarian xenografts, and cell line tumour implantation models of prostate and breast cancer. DNA was isolated from DBS and size-selected using cumulative cycles of bead-based purification to remove genomic DNA. Libraries generated from size-selected eluates were submitted for paired-end, shallow whole genome sequencing (sWGS) at depth of ~1x. Using established bioinformatic pipelines, ichorCNA, t-MAD, and Xenomapper, sWGS data were analysed for somatic copy number aberrations (SCNAs) and tumour fraction (TF), and compared to data from primary tumour samples, clinical parameters as well as data from volumetric, metabolic, or photoacoustic imaging.

Results

Using sWGS data, we detected SCNAs in fpDBS corresponding to primary tumour tissue (available from 8/10 patients) in > 60% of the late-stage oesophageal cancer patients (5/8). Analysis of ctDNA levels in serial DBS of human and mouse revealed changes in TF reflecting observed clinical measurements and imaging modalities.

Conclusion

Our data suggest that in the appropriate settings, the analysis of ctDNA from DBS can be used for the detection of cancer, molecular profiling of SCNAs and for tumour monitoring, in cancer patients and pre-clinical models. DBS TF at investigated time points can reflect disease progression or treatment response. These preliminary results imply that DBS-based ctDNA assays may be used as an additional tool in clinical trials for disease surveillance and prediction of disease outcome.