MICROFLUIDICS

Exploring Diagnostic And Prognostic Biomarkers for Targeted Therapy

Bogdanova, N.V. et al. “The prognostic value of liquid biopsies for benefit of salvage radiotherapy in relapsed oligometastatic prostate cancer.” *Cancers* 14 (2022): 4095. doi.org/10.1093/noajnl/vdaf015.

Identifying patients who will benefit from targeted therapies before initiating treatment is critical to extending progression-free survival in relapsed cancer. Researchers from Hanover Medical School in Germany used circulating tumor cells and total RNA enriched from liquid biopsies of men with oligometastatic prostate cancer relapse to identify mRNA “transcriptional signatures” that correlated with known tissue-specific markers of tumor aggressiveness. Evaluation of relative transcript levels was enabled by high-throughput microfluidic quantitative real-time PCR (qRT-PCR) on the Standard BioTools™ Biomark™ platform. This demonstrated the clinical value of quantifying blood-derived RNAs to identify patients who received benefit from intervention and supports expansion of novel diagnostic and prognostic biomarkers of treatment response.

Key takeaways

- Tumor cells and total RNA were obtained from noninvasive liquid biopsies, and quantification of transcript levels was enabled by the Biomark platform
- Distinct transcriptional signatures were found in patients who experienced short- and/or long-term benefit from radiotherapy
- Transcript levels were significantly correlated with common tumor tissue assessments such as Gleason score and TNM classification
- Implications for pharma: In the era of individualized treatment programs, validated biomarkers to guide intervention decisions are required
- A high-throughput and automated Biomark platform and Delta Gene™ assays (both from Standard BioTools) provided a cost-effective and time-saving approach for gene expression profiling

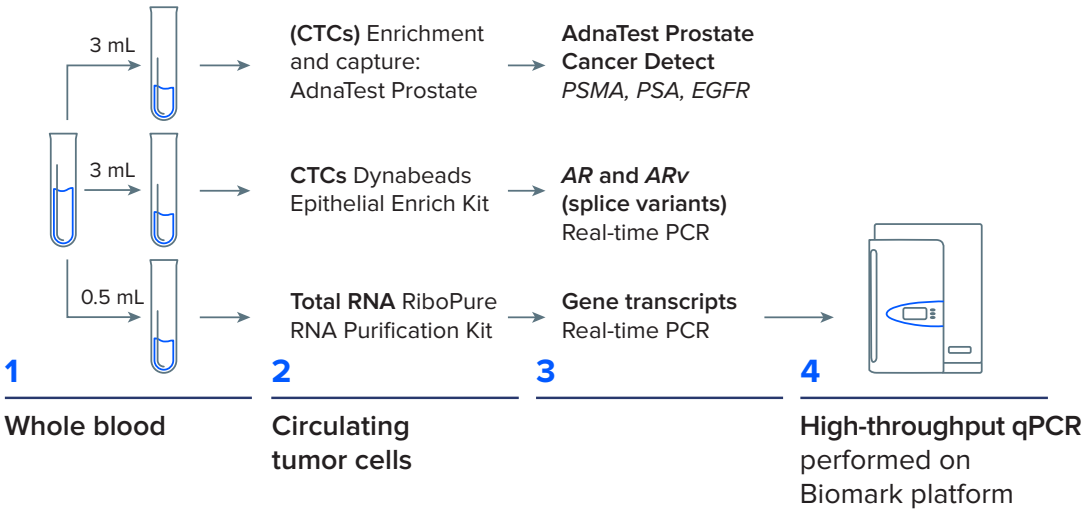

Figure 1. Study overview

Background

Many prostate cancer patients relapse after initial curative therapy, indicated by rising PSA levels. In oligometastatic relapse, tumor tissue for treatment decision-making is often unavailable, which underscores the need for liquid biopsy-based predictive tests. PSA alone is a poor biomarker because it cannot fully capture tumor burden, metastatic stage or treatment benefit/failure. Validated biomarkers that are prognostic and predictive of treatment response are required in this age of individualized oncology prescription.

Study design

Total RNA was isolated from blood and processed for cDNA synthesis from 43 patient samples. All experiments included quadruplicate samples and controls. In total, 54 gene candidates from the most representative signaling pathways were selected for this study using various technologies and platforms. A subset of 34 genes were analyzed on the Biomark platform using Delta Gene assays (via the Standard BioTools D3™ custom assay design tool) and the 96.96 Dynamic Array™ integrated fluidic circuit (IFC). The authors identified candidate biomarkers superior to PSA in clinical determination of patients who would see improved progression-free survival with radiotherapy.

Results

- Distinct transcriptional signatures were found in patients who experienced short- and/or long-term benefit from radiotherapy, and seven transcripts were associated with disease remission (Figure 2)
- Several transcripts were significantly correlated with validated clinical tumor indices such as Gleason score and TNM classification

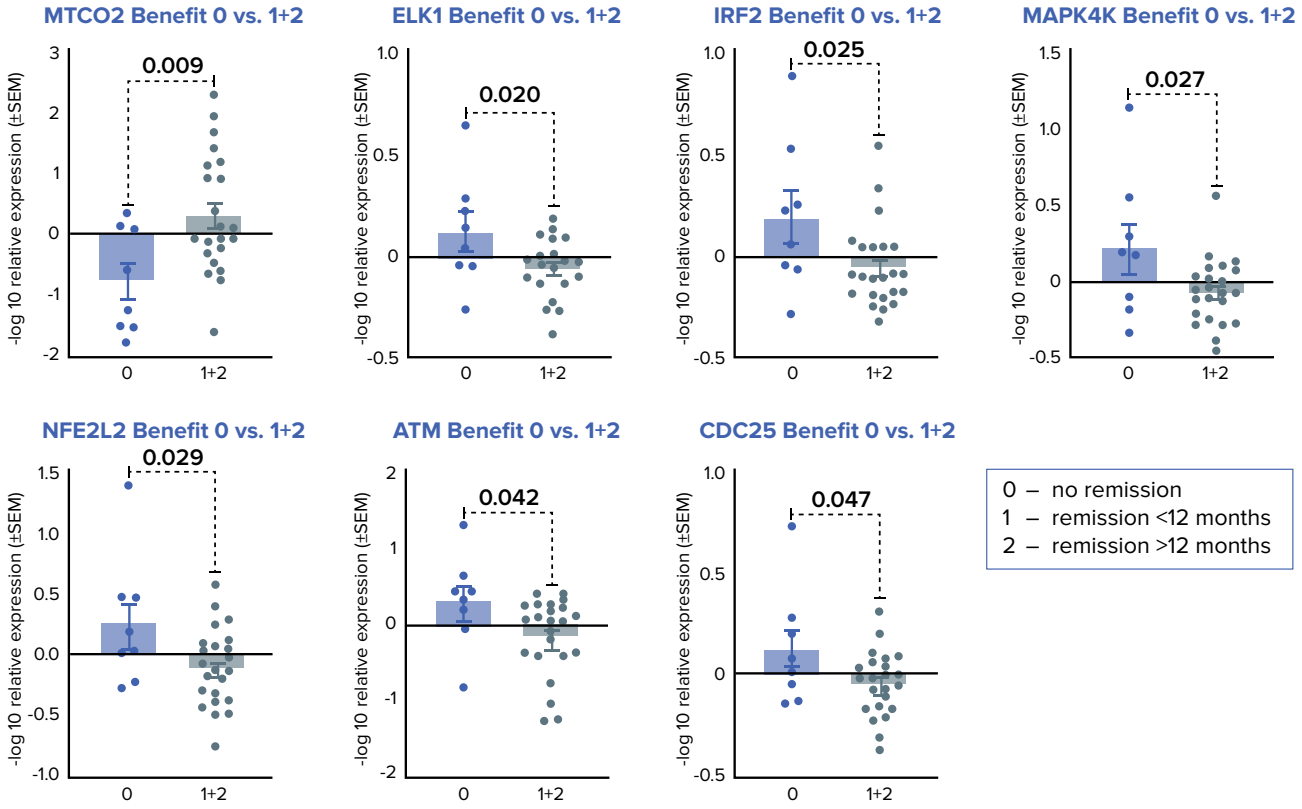

Figure 2. Seven transcripts (*MTCO2, ELK1, IRF2, MAPK4K, NFE2L2, ATM* and *CDC25*) were significantly associated with disease remission.

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