GALEAS® Tumor

A novel comprehensive solution to clinicial genetic tumor profiling

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Introduction

Cancer is the second most frequent cause of death worldwide[1]. Numerous types and subtypes of cancer exist, and there is no single pathway responsible for initiating disease onset. Instead, cancers are driven by a myriad of genomic alterations, and their differing combinations impact an individual cancer's initiation, development and response to treatment.[2]

Genomic profiling and use of biomarkers including microsatellite instability (MSI) status or Tumor Mutational Burden (TMB) scores can inform scientists and clinicians about tumor genomic profiles and help direct therapeutic strategies. Therefore, it is vital that comprehensive genomic profiling delivers clinically relevant information.

To enable clinicians and researchers access to this comprehensive analysis, Nonacus introduces GALEAS® Tumor. GALEAS® Tumor provides a cost effective workflow for the profiling and analysis of single nucleotide variants (SNVs) and copy number variants (CNVs) in 519 highly curated, clinically relevant genes as well as providing a measure for genome wide copy number alterations, TMB and MSI status.

The GALEAS® Tumor workflow has been validated on reference samples, 50 FFPE colorectal cancer samples and 50 FFPE healthy donor samples.

Methods

The following FFPE DNA clinical samples (100-200ng per sample) and reference standards (50ng per Sample) were processed to demonstrate clinical utility of GALEAS® Tumor:

- 50 colorectal cancer (CRC) patient samples from FFPE
- 50 normal samples from FFPE
- Reference standard material from FFPE and gDNA including SNV, INDEL, CNV, MSI, TMB

Libraries were prepared using the GALEAS® Tumor Hybridization and Capture Enrichment kit and sequenced on an Illumina Sequencer to a mean coverage of 500x, requiring only 4Gb of data.

Data analysis was performed through the GALEAS® Analysis Software, a cloud-based solution for the analysis of the GALEAS® Tumor Panel.

GALEAS® Tumor provides innovative support, analysis and optimized variant detection for primary tumor screening. The solution delivers an integrated platform for cancer care ensuring clinicians get access to comprehensive bioinformatics analysis aiding diagnosis, guiding appropriate treatment and ultimately improving the patient outcome.

Panel Validation SNV, INDEL and CNV

Assay performance was validated using the Galeas® Analysis Software with a Limit of Detection (LoD) of 5% at 500x. The efficacy of the GALEAS® Tumor workflow was assessed using reference material from FFPE containing 23 SNVs and INDELs that had previously been confirmed by ddPCR. Variant calling results show detection of SNV and INDELs with a recall of 100%. Variant calls accurately reflect expected allele frequencies.

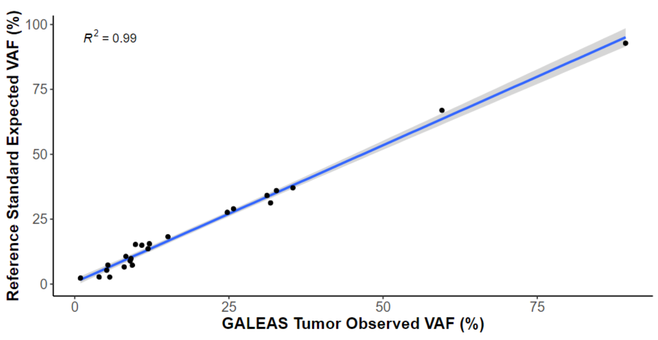

Figure 1. SNV and INDEL recall rate for alterations in reference material from FFPE.

Reference gDNA samples with known aberrations were sequenced to a mean coverage of 500x and used to evaluate the somatic CNV calling performance of the GALEAS® Tumor workflow at the gene level. Figure 2 shows detection of aberrations in the genes of interest that reflect the reported copy numbers.

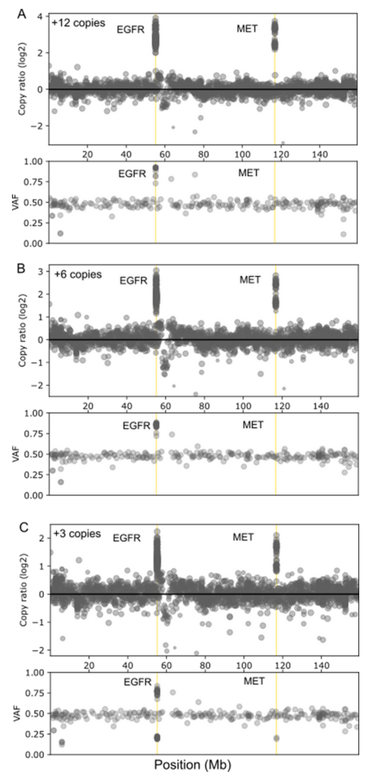

Figure 2. Validating gene level CNV calls with a CNV Lung and Brain Mix reference standard at 12 (A), 6 (B) and 3 (C) copies. Genes highlighted here are EGFR and MET.

CRC Cohort Summary

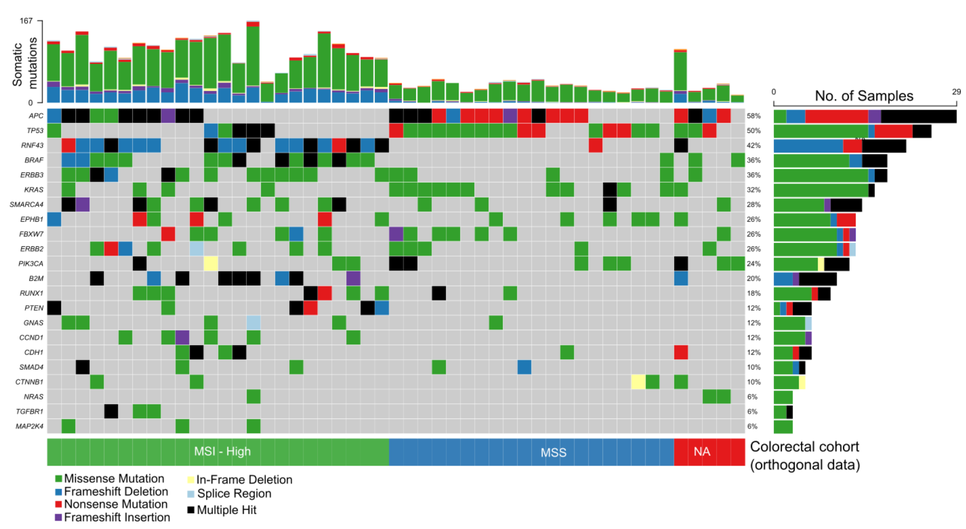

Figure 3. Oncoplot from 50 CRC cohort highlighting detection of somatic mutations from a tumor only approach in genes with known cancer hotspots to demonstrate overall performance of GALEAS® Tumor.

Genome Wide CNV Detection

The design of the GALEAS® Tumor solution allows accurate profiling of clinically relevant large aberrations using a high-density genome wide SNP backbone along with the panel gene content.

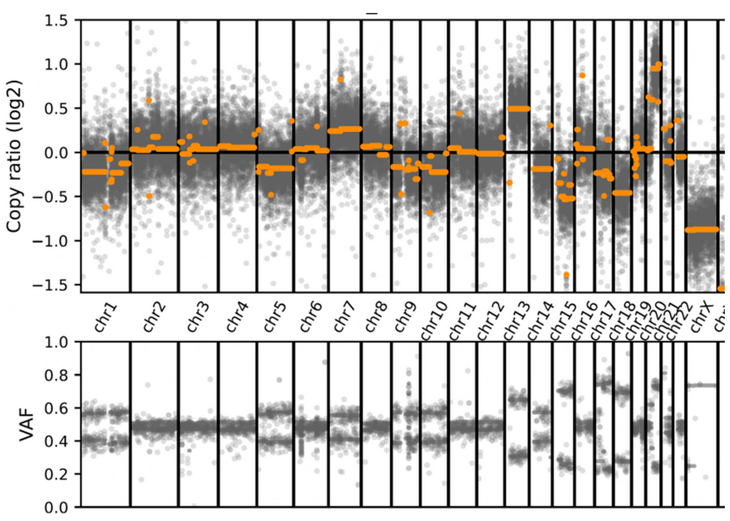

Figure 4. CRC sample run with GALEAS® Tumor workflow demonstrating a genome wide copy number profile derived from the gene content and SNP-backbone.

MSI

GALEAS® Tumor enables comprehensive detection of MSI. Samples with known MSI status were tested with the GALEAS® Analysis Software which accurately called the MSI and MSS FFPE reference controls; 100% of confirmed MSS FFPE cancer and normal samples; and 23/24 confirmed MSI FFPE cancer samples (Fig 5).

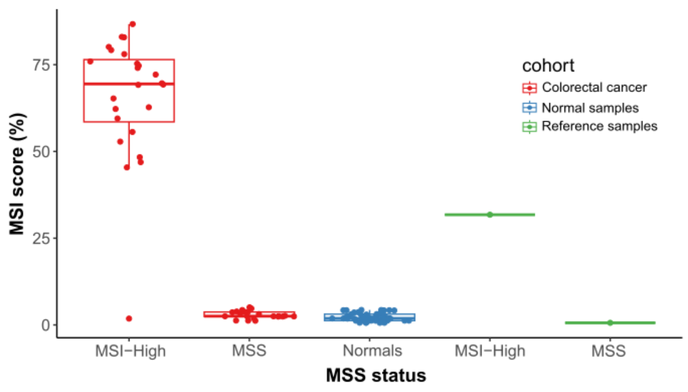

Figure 5. Comparisons of GALEAS® Tumor MSI scores with known MSI status from CRC primary tumor FFPE samples (MSI-High), healthy individuals (MSS) and reference standards.

TMB

TMB is a key immuno-oncology marker and correlates with MSI status. The performance of GALEAS® Tumor was assessed by comparing the TMB score generated by the GALEAS® analysis software, to known MSI status in the cohort of colorectal cancer samples. We demonstrate that calling TMB with the GALEAS® tumor workflow correlates highly with MSI status and that TMB low and high reference standards scores were correctly called (Fig 6).

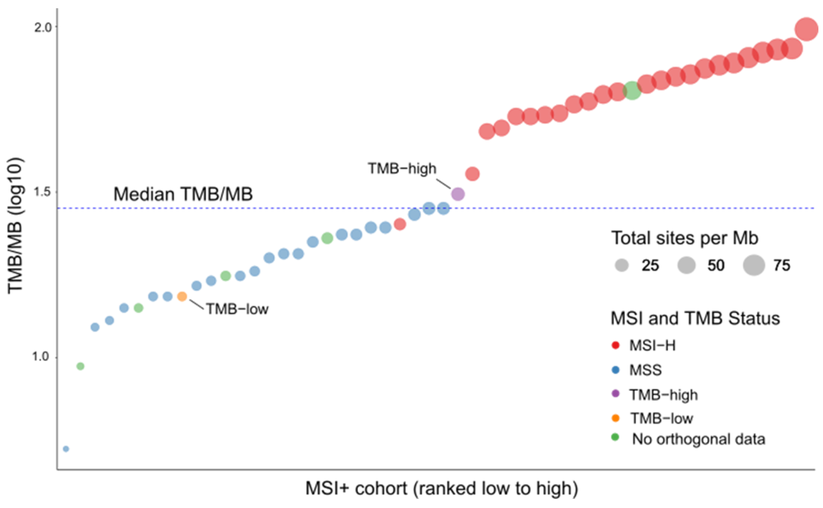

Figure 6. GALEAS® Tumor TMB scores across 50 CRC samples and compare with MSI Status.

Summary

GALEAS® Tumor allows the profiling and analysis of over 500 clinically relevant genes, along with cancer-specific biomarkers to help in the diagnosis and treatment of patients with cancer.

GALEAS® Tumor is designed to maximize the diagnostic yield from low DNA inputs. This provides a comprehensive, simple, wet-lab and bioinformatic solution for the accurate detection of oncogenic variants including SNV/INDELs, CNV, MSI and TMB.

References:
1. Ciriello G., Miller ML., Askoy BA., Senbabaoglu Y., Schultz N., Sander C. "Emerging landscape of oncogenic signatures across human cancers." Nature genetics (2013): 1127-1133.
2. The ICGC/TCGA PanCancer Analysis of Whole Genomes Consortium. "Pan-cancer analysis of whole genomes." Nature (2020): 82-93.

Key Points

GALEAS® Tumor is a cost-effective solution for streamlining the profiling of solid tumors, providing clinicians with comprehensive analysis of SNVs INDELS, CNV, MSI and TMB.

100% coverage of the NHS National Genomic Test Directory for Cancer.

The GALEAS® Analysis Software allows the sensitive and accurate detection of clinically relevant markers in even the most challenging sample types.

The technology underlying GALEAS® Tumor can be used to profile ctDNA; allowing solid tumor screening from liquid biopsy samples, when a viable solid tumor biopsy can't be obtained.