
NORTHSTAR
Treat. Monitor. Adapt.
With Molecular Precision.
Northstar Select™
Liquid Biopsy with
More Treatment Options,
More Often
Northstar Response™
Precise, Tissue-Free
Treatment Response
Monitoring

MOLECULAR
PRECISION
AT EVERY STEP

Treat.
Monitor.
Adapt.

SELECT

Liquid Biopsy with More Treatment Options, More Often

A tissue-free, ultra-sensitive, 84-gene genomic alteration panel with MSI status. The panel covers all solid tumors alterations associated with FDA-approved targeted therapies and immunotherapies, and provides clinical trial matching.

- 82 genes for single nucleotide variants (SNVs) / indels
- 19 genes for copy number amplifications
- 5 genes for copy number loss
- 9 genes for fusions

An alternative to tissue

Tissue samples tend to fail at a higher rate, increase TAT, and may not be representative of the entire tumor / malignancy.

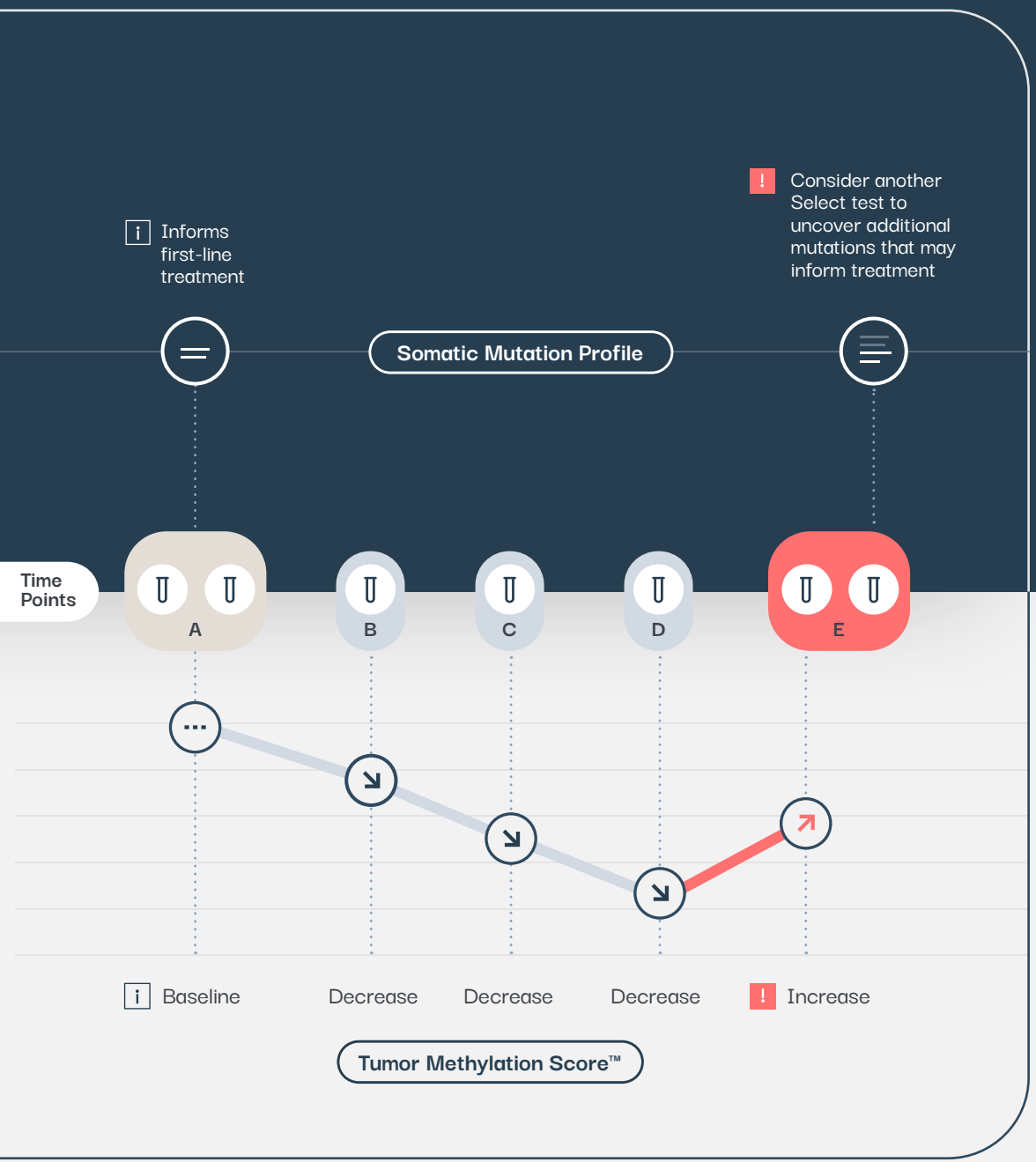
Precise, Tissue-Free Treatment Response Monitoring

Analyzes >500 genomic loci uniquely methylated in cancer cells. Utilizes methylation signature to estimate tumor fraction. A Tumor Methylation Score™ on each report is used to quantify changes in molecule count, enabling treatment response monitoring. The change in methylated tumor molecules across time points can help understand how the tumor is evolving.

A complement to imaging

Imaging interpretation can be confounded by immunotherapy pseudo-progression.

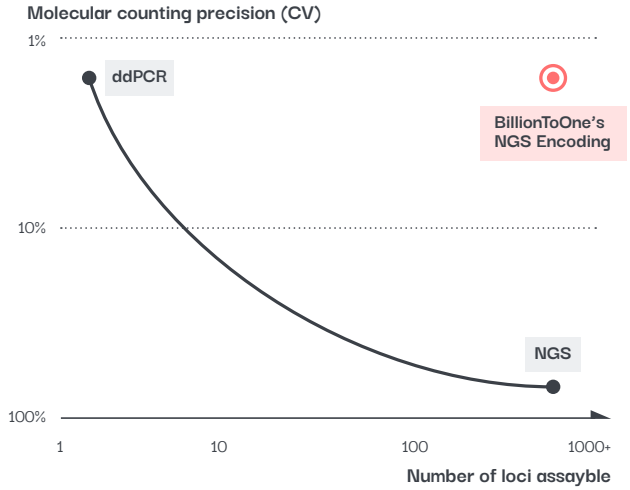
RESPONSE



THE TECHNOLOGY

Single-molecule level quantification powered by patented Quantitative Counting Templates™ (QCT™)

BillionToOne's QCT™ technology combines the sensitivity of ddPCR with the breadth of NGS, enabling precise quantification and ultra-senstive detection of low variant allele fraction (VAF) actionable targets.



SELECT Treat more actionable mutations with ultra-sensitive genomic profiling.

Druggable mutations are actionable at very low VAF. Uncover more treatment options with an ultra-sensitive assay that offers an extremely low limit of detection (LOD). Studies have shown patients with very low-VAF (<0.2%) mutations responded to therapy[1,2].

50% of alterations fall below 0.5% VAF and are challenging to detect[3]:

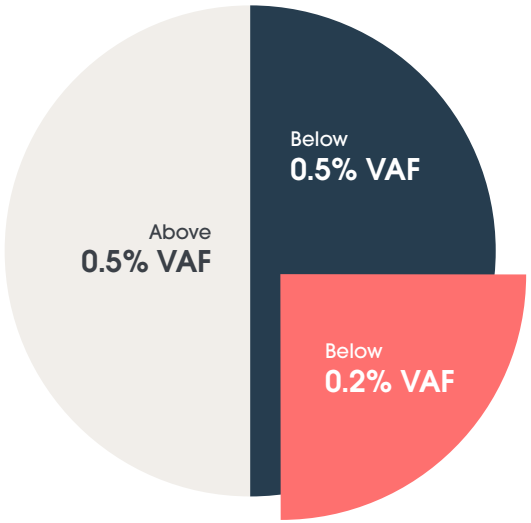


Figure 1. A survey of >1,000 plasma samples found that half of all detected SNVs occurred below ~0.5% VAF ●, and a quarter were below 0.2% VAF ●. Variant detection was generally unreliable and variable between assays for alterations lower than 0.5% VAF.[3]

Northstar Select offers ~2X lower LOD[4], making it possible to uncover more actionable alterations:

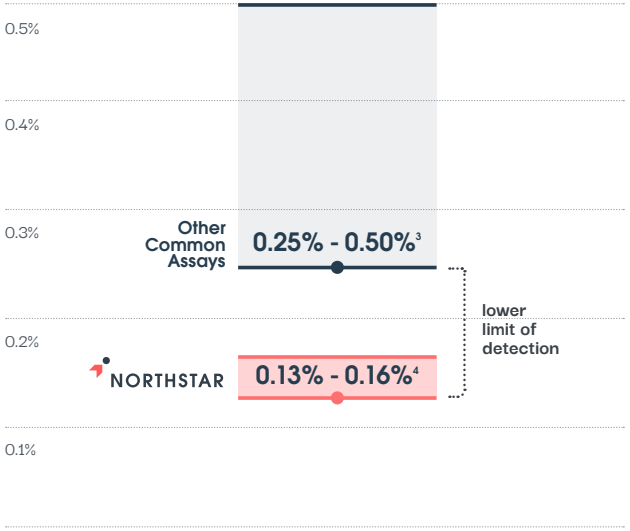


Figure 2. Cited LODs of common assays in the market range from 0.25% to 0.50%[3] ●. Northstar Select's LOD ranges from 0.13% to 0.16%[4] ●. LOD is defined as the lowest concentration of an analyte in a sample that can be consistently detected with ≥95% probability.

1. Abida W, Armenia J, Gopalan A, et al. Prospective Genomic Profiling of Prostate Cancer Across Disease States Reveals Germline and Somatic Alterations That May Affect Clinical Decision Making. JCO Precis Oncol. 2017;2017:PO.17.00029. doi:10.1200/PO.17.00029
2. Jacobs MT, Mohindra NA, Shantzer L, et al. Use of Low-Frequency Driver Mutations Detected by Cell-Free Circulating Tumor DNA to Guide Targeted Therapy in Non-Small-Cell Lung Cancer: A Multicenter Case Series. JCO Precis Oncol. 2018;2:1-10. doi:10.1200/PO.17.00318
3. Deveson IW, Gong B, Lai K, et al. Evaluating the analytical validity of circulating tumor DNA sequencing assays for precision oncology. Nat Biotechnol. 2021;39(9):1115-1128. doi:10.1038/s41587-021-00857-z
4. Internal validation data. June 2023

Alteration Type	Reportable Range	Allele Fraction / Copy Number	Analytical Sensitivity	Analytical Specificity
SNVs / Indels	≥0.01%	>0.17% 0.13 - 0.16% 0.06 - 0.12%	>99% 95.5% 78.4%	>99.9%
CNAs*: Amplifications	≥2.1 copies**	2.125 - 2.160 copies***	95%	
CNAs*: Losses	≤1.9 copies	≥1.77 copies	>95%	
Fusions	≥0.02%	>1%	>99%	
MSIs	n/a	0.07%*** >0.4%	95% 100%	

Ultra-Sensitive Detection

* This translates to variant detection at a 0.02 - 0.04% allele fraction even with limited DNA input quantities (i.e. 15 - 30ng of cfDNA).
** 2.5% tumor fraction at 6 copies of amplification. *** Impacted by biological variability.

Table 1. Northstar Select's performance specifications. Internal data on file, June 2023.

SNVs / Indels 82 genes

AKT1	*CCNE1*	*EZH2*	*JAK2*	*NOTCH1*	*RET*
AKT2	*CD274* (PD-L1)	*FANCA*	*JAK3*	*NPM1*	*RHOA*
ALK	*CDH1*	*FBXW7*	*KIT*	*NRAS*	*RIT1*
APC	*CDK12*	*FGFR1*	*KRAS*	*NTRK1*	*ROS1*
AR	*CDK4*	*FGFR2*	*MAP2K1* (MEK1)	*PALB2*	*SF3B1*
ARAF	*CDK6*	*FGFR3*	*MAP2K2* (MEK2)	*PDGFRA*	*SMAD4*
ARID1A	*CDKN2A*	*FGFR4*	*MET*	*PIK3CA*	*SMO*
ATM	*CDKN2B*	*GATA3*	*MLH1*	*PMS2*	*STK11*
BRAF	*CHEK2*	*GNA11*	*MPL*	*PTEN*	*TERT*
BRCA1	*CTNNB1*	*GNAQ*	*MSH2*	*PTPN11*	*TP53*
BRCA2	*DDR2*	*GNAS*	*MSH6*	*RAD51C*	*TSC1*
BRIP1	*EGFR*	*HRAS*	*MTOR*	*RAD51D*	*VHL*
CCND1	*ERBB2* (HER2)	*IDH1*	*MYC*	*RAF1*	
CCND2	*ESR1*	*IDH2*	*NF1*	*RB1*	

CNAs: Amplifications 19 genes

AR	*ESR1*	*PIK3CA*
BRAF	*FGFR1*	*RAF1*
CCNE1	*FGFR2*	*RET*
CD274 (PD-L1)	*KIT*	
CDK4	*KRAS*	
CDK6	*MET*	
EGFR	*MYC*	
ERBB2	*PDGFRA*	

CNAs: Losses 5 genes

ATM	*CDKN2A*
BRCA1	*PTEN*
BRCA2	

Fusions 9 genes

ALK
BRAF
FGFR2
FGFR3
NTRK1
NTRK2
NTRK3
RET
ROS1

Biomarker

Microsatellite Instability Status (MSI)

Table 2. Northstar Select's gene list.

MORE TREATMENT OPTIONS, MORE OFTEN

Monitor treatment response precisely and adapt your strategy.

THE POWER OF METHYLATION

This NGS-based test is designed to detect hundreds of genomic loci uniquely methylated in cancer cells. Northstar Response measures the change in methylated tumor molecules, reflecting tumor fraction changes with high accuracy.

>10x stronger signal than SNV-based ctDNA monitoring assays.

Distinct from a limited number of single nucleotide variants (SNVs), which are commonly used for ctDNA monitoring, Northstar Response interrogates >500 cancer-associated, hypermethylated genomic loci which represents more than 10x the targets. QCT technology combined with the high number of loci and personalized germline filtering enables highly precise quantification.

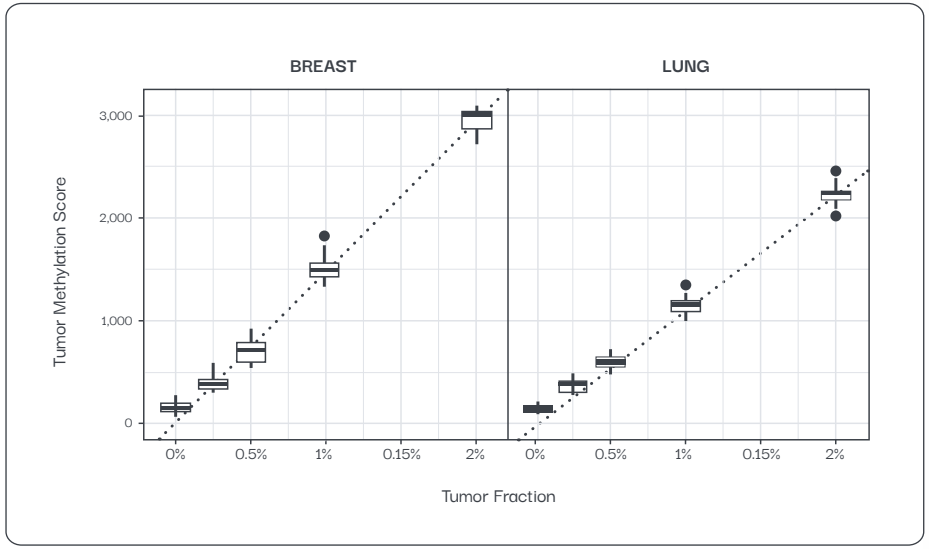


Figure 3. Median and interquartile range of Tumor Methylation Scores at each tumor fraction. Sheared gDNA from tumor cells were added to sheared gDNA from healthy cells from the same subject at different tumor fraction.

CLINICAL RELEVANCE

Northstar Response can aid in the detection of progression.

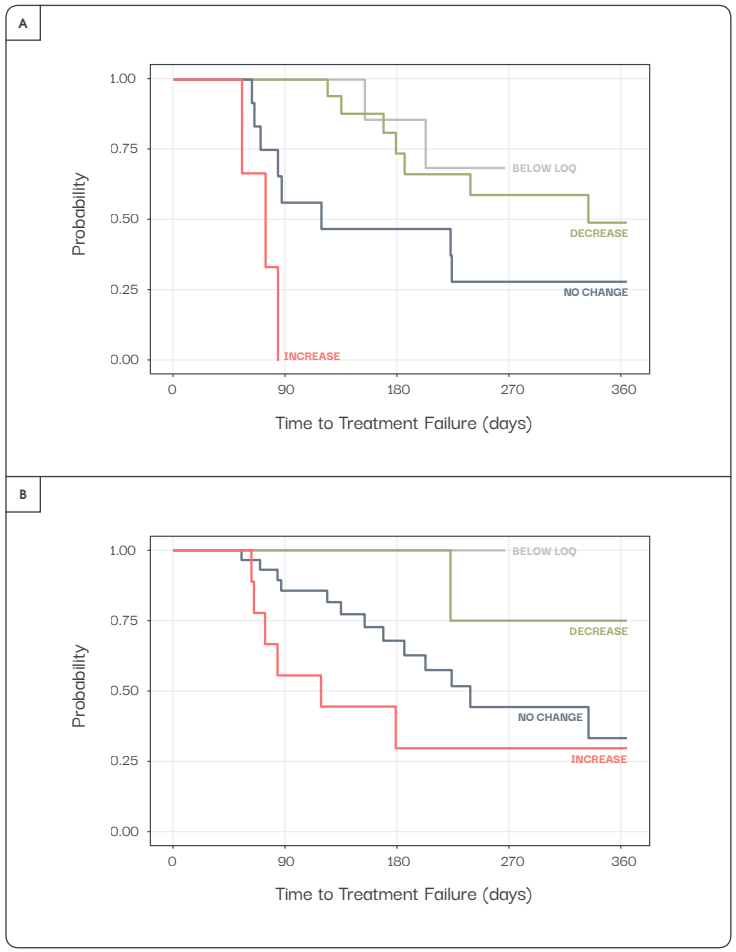


Figure 4. Northstar Response successfully stratifies ICI immunotherapy clinical outcomes. (A) Change in Tumor Methylation Score from pre-treatment to post-treatment 1, $p < 0.0001$. **(B)** RECIST at post-treatment 1, $p = 0.14$.

Source: Ye et al. Methylated ctDNA dynamics correspond with clinical tumor load in metastatic lung cancer patients on therapy. Poster presented at: AACR 2023; April 18, 2023; Orlando, FL. Abstract 5588.

MONITOR + ADAPT WITH PRECISION GUIDANCE

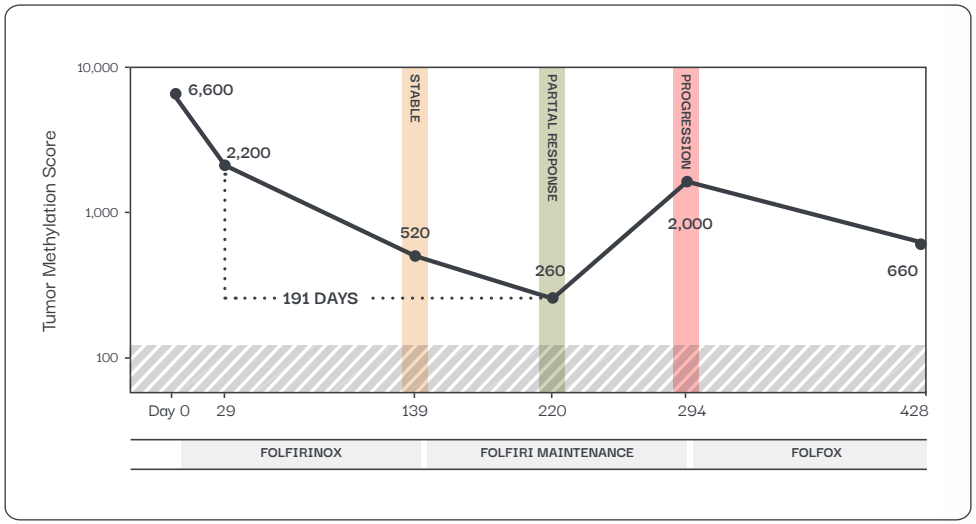
CASE EXAMPLE 01

Detected partial response 191 days before imaging and subsequently detected progression

Stage IV Pancreatic Ductal Adenocarcinoma

Chemotherapy

- folfirinox
- followed by folfiri maintenance
- followed by folfox



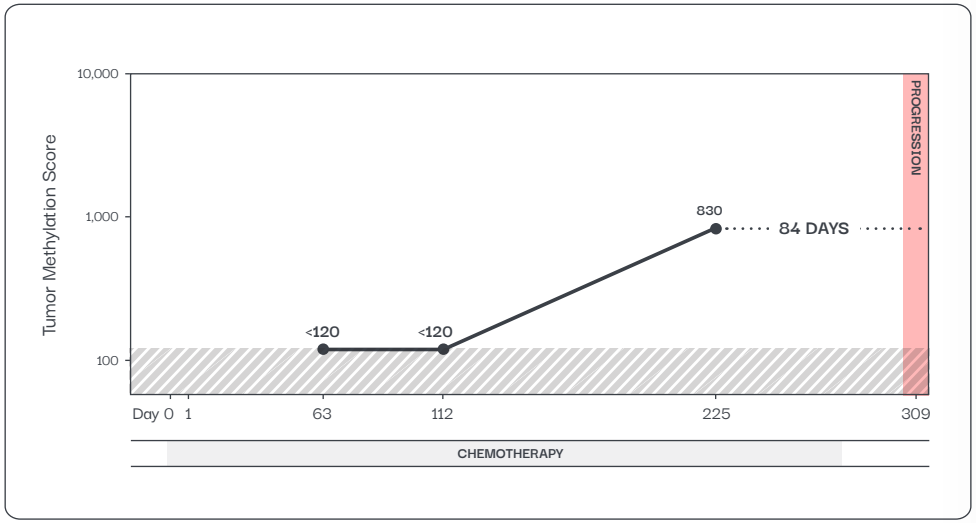
CASE EXAMPLE 02

Detected ctDNA increase 84 days before imaging detected progression

Stage IV Colorectal Adenocarcinoma

Chemotherapy + Immunotherapy

- fluorouracil / leucovorin / bevacizumab



Ease of access to providers and patients

- ✔ Whole blood sampling, no tissue required
- ✔ Appropriate for any late stage solid tumor type
- ✔ Informs and monitors response to targeted therapy & immunotherapy
- ✔ Clear reporting with ~2 week TAT from lab receipt

BillionToOne is committed to making Northstar assays accessible to patients. We have a robust financial support program available and a dedicated billing support team to help answer questions and resolve any concerns. For any questions, please call 833-537-1819 or email support@northstaronc.com.

BILLIONTOONE

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BillionToOne is a precision diagnostics company founded in 2016 with the mission to make molecular diagnostics more accurate, efficient, and accessible for all. The CLIA-licensed laboratory is based in Menlo Park, CA. BillionToOne has commercialized a series of unique cell-free DNA-based assays, including the first and only single-gene non-invasive prenatal test for recessive conditions and red blood cell fetal antigens, and therapy selection and response monitoring liquid biopsy assays.

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