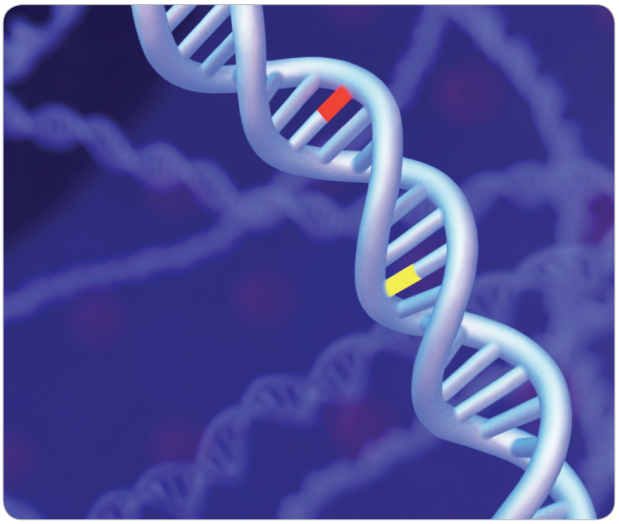
nCounter® Vantage 3D™

DNA SNV Solid Tumor Panel



Simplify Tumor Characterization with Multiplexed Detection of Cancer Driver Mutations

The nCounter® Vantage 3D™ DNA SNV Solid Tumor panel simplifies solid tumor mutation detection, while providing sensitive and specific results. This highly multiplexed assay is capable of simultaneously characterizing single nucleotide variants (SNV) and small InDels from as little as 5 ng of DNA from FFPE samples in a single tube. Powered by nCounter technology, which employs amplification-free direct digital counting, detection of mutant and reference alleles is highly sensitive (>95%) and specific (>95%) down to somatic allele frequencies of 5%. Designed with 3D Biology™ technology, the Vantage 3D DNA SNV panel, delivers reliable SNV detection that may be combined with mRNA, Fusion Genes and Protein detection to take your tumor characterization deeper.

Product Highlights

Maximum information from limited samples: 5 ng of input DNA for SNV and InDel detection

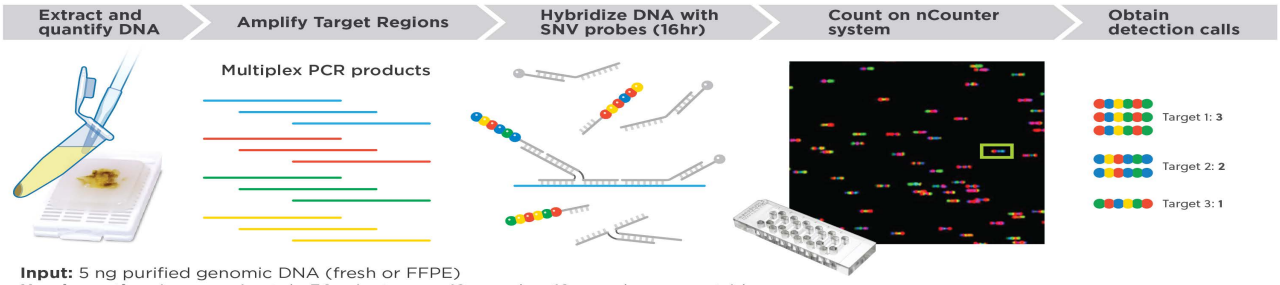
- Simple protocol, optimized for challenging FFPE samples.
- Highly sensitive (>95%) and specific detection (>95%) of cancer driver mutations.
- Simple, integrated data analysis, eliminating the need for a bioinformatician.
- Customizable and forward-compatible with our growing line of 3D Biology Products.

Assay Details

Feature	Specification
Input Material	5 ng genomic DNA
Hands on Time	~30 minutes
Time to Results	<24 hours
Sample Type(s)	FFPE, fresh frozen tissue, cell extracts, cell lysates
Data Analysis	nSolver™ Analysis 4.0 (Research use only)

Simple Digital Cancer Driver SNVs and Short InDel Detection

Eliminate library prep, sample input/type limitations and data analysis hurdles found with NGS



Input: 5 ng purified genomic DNA (fresh or FFPE)
Hands-on-time is approximately 30 minutes per 12 samples; 12 samples per cartridge
Sample-to-answer time depends on purifying and quantifying the DNA; ranges from 2-3 days

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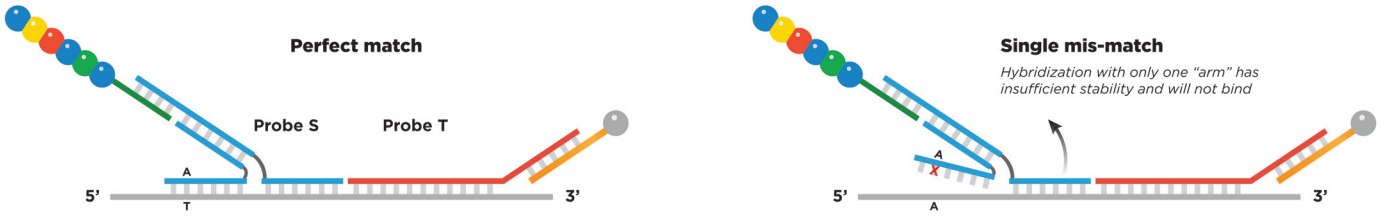
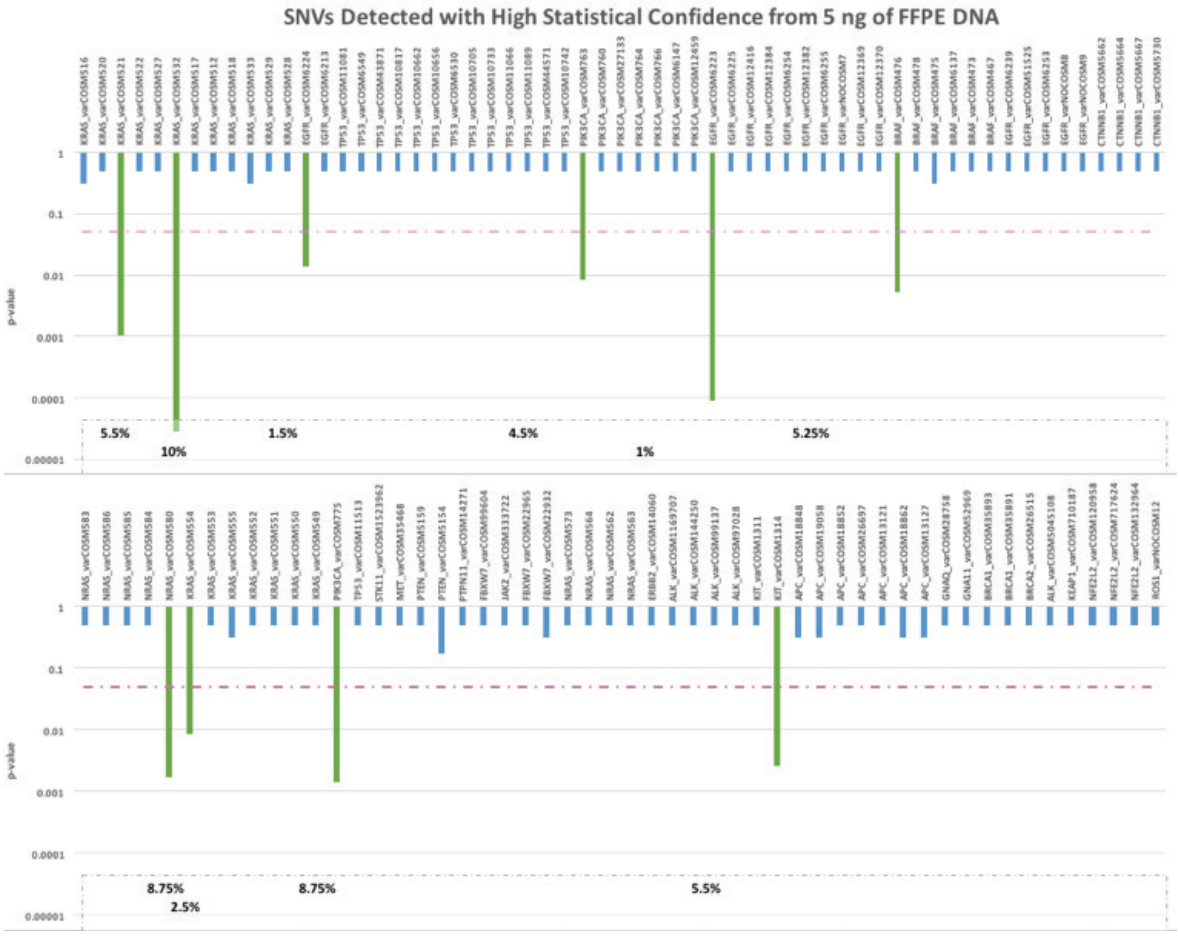
Highly Specific Detection with Single-Base Resolution

The nCounter Vantage 3D DNA SNV Solid Tumor Panel employs a unique probe design that enables highly specific, >95%, detection of mutation sequences with >95% sensitivity down to somatic allele frequencies of 5%. Each SNV assay is designed to detect the mutant allele of interest and a reference allele using a set of probes with novel architecture. The upstream probe (Probe S) has proprietary sequences that become unstable in the presence of a single nucleotide mismatch. The downstream probe (Probe T) is based on existing NanoString probe chemistry. Pools of Probe S and T are combined with an nCounter molecular barcode SNV TagSet to enable highly specific detection of single nucleotide variants in a background of abundant normal tissue alleles.



Variants present at 1–10% levels are detected from 5 ng of FFPE DNA

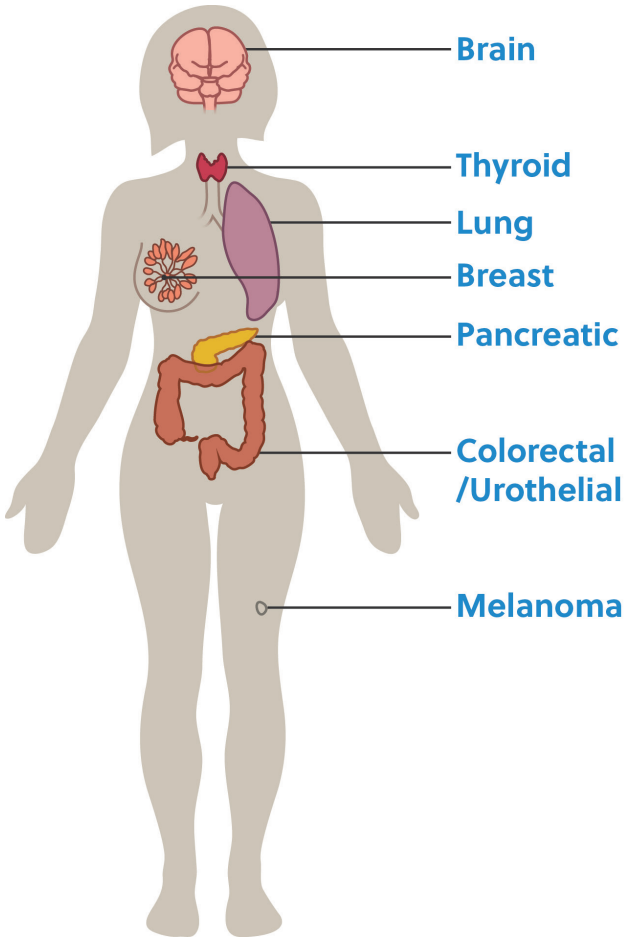
Here the sample was 5 ng of genomic DNA extracted from FFPE sections purchased from Horizon Discovery and blended to contain 10 different variants ranging in frequency from 1% to 10%. All assayed variants are detected with >95% confidence (p<0.05 confidence threshold indicated by the dashed pink line).



Detect Mutations That Provide Translational Research Insights

The nCounter Vantage 3D DNA SNV Solid Tumor Panel has been carefully curated for labs with a translational research focus. Designed to identify the most meaningful variants across a variety of solid tumor types, this panel includes somatic variants associated with lung adenocarcinoma, thyroid carcinoma, pancreatic adenocarcinoma, colorectal adenocarcinoma and melanoma. The content was determined through a rigorous process of selection from various databases and input from industry leaders. The genes and mutations covered are relevant to new and existing clinical trials, drug pipelines, tumor subtypes, and drug resistance and response.

Genes represented in the Vantage 3D DNA SNV Panel	
ALK	KEAP1
APC	KIT
BRAF	KRAS
BRCA1	MET
BRCA2	NFE2L2
CTNNB1	NRAS
EGFR	PIK3CA
ERBB2	PTEN
FBXW7	PTPN11
FGFR2	ROS1
GNA11	STK11
GNAQ	TP53
JAK2	



Highly Optimized for Use with Only 5 ng of DNA in Wide Range of FFPE Samples

In collaboration with a team from The University of Texas MD Anderson Cancer Research Center, 5 ng of purified genomic DNA from >40 different FFPE clinical research samples from a variety of cancer types were assayed with the nCounter SNV detection chemistry. DNA integrity scores (DIN from TapeStation 2200 analysis) ranged from 2.3 to 6.1 for these samples. Somatic variants that had been previously detected by next-generation sequencing were detected with 98.1% sensitivity, 100.0% specificity, and 99.9% accuracy. Representative results for a selection of these samples are shown in Table 1.

Table 1: Somatic mutations associated with cancer were detected from small amounts (5 ng) of FFPE DNA with high sensitivity (>95%), high specificity (>99%), and high accuracy (>99%) for a range of cancer-types and samples as compared to mutations detected by targeted deep-sequencing. Samples provided by the Institute for Personalized Cancer Therapy – MD Anderson Cancer Center.

Sample Name	Expected Mutation(s) identified by NGS	COSMIC ID	Variant Allele Frequency by NGS	SNV(s) detected by nCounter	DNA Quality (DIN)	Cancer Type	Primary or Metastatic
FFPE-01	APC_R876	COSM18852	33.6%	Y	4.2	Anal Cancer	Distant Mets
FFPE-02	KRAS_G12V	COSM520	10.8%	Y	3.7	Pancreatic	Distant Mets
FFPE-03	KRAS_G12D / APC_I1307K	COSM521 / COSM26697	15.5% / 42.7%	Y / Y	3.8	Melanoma	Distant Mets
FFPE-04	KRAS_G13D	COSM532	10.0%	Y	2.9	Colorectal	Primary
FFPE-05	KRAS_G12C / CTNNB1_T41A	COSM516 / COSM5664	15.37% / ?	Y / Y	2.4	Colorectal	Primary
FFPE-06	KRAS_G12A	COSM522	32.6%	Y	2.8	Lung	Primary
FFPE-07	NRAS_Q61K	COSM580	23.7%	Y	5.5	Melanoma	Primary
FFPE-08	NRAS_Q61L / PIK3CA_E542K	COSM583 / COSM760	46.51% / 12.28%	Y	3.3	Colorectal	Primary
FFPE-09	NRAS_61R	COSM584	55.3%	Y	4.7	Melanoma	Distant Mets
FFPE-10	NRAS_Q61H / NRAS_Q61R	COSM586 / COSM584	33.6% / 34.0%	Y	4.4	Melanoma	Distant Mets
FFPE-11	PIK3CA_H1047R	COSM775	14.8%	Y	3.2	Brain	Primary
FFPE-12	BRAF_V600E	COSM476	12.4%	Y	6.1	Melanoma	Primary
FFPE-13	APC_I1307K	COSM26697	17.7%	Y	4.2	Colorectal	Primary
FFPE-14	APC_R564 / KRAS_G13D	COSM18848 / COSM532	8.3% / 20.0%	Y / Y	3.6	Colorectal	Distant Mets
FFPE-15	APC_R876 / KRAS_G12D	COSM18852 / COSM521	5.4% / 10.5%	Y / Y	3.4	Colorectal	Distant Mets
FFPE-16	APC_Q1367 / BRAF_V600E	COSM13121 / COSM476	13.4% / 14.6%	Y / Y	3.5	Colorectal	Primary
FFPE-17	KRAS_G12S / APC_Q1378	COSM517 / COSM18862	22.6% / 11.9%	Y / Y	3.3	Sacroma	Primary
FFPE-18	BRAF_V600E	COSM476	5.9%	Y	4.7	Melanoma	Primary
FFPE-19	BRAF_K601E	COSM478	18.9%	Y	1.7	Melanoma	Distant Mets
FFPE-20	BRAF_V600K	COSM473	31.1%	Y	6.9	Melanoma	Distant Mets
FFPE-21	CTNNB1_S45F / NRAS_Q61L	COSM5667 / COSM583	5.9% / 16.5%	Y / Y	3.2	Melanoma	Distant Mets
FFPE-22	CTNNB1_T41A / KRAS_G12V	COSM5664 / COSM520	33.2% / 20.5%	Y / Y	5.9	Colorectal	Distant Mets
FFPE-23	NRAS_Q61H	COSM586	39.3%	Y	2.2	Melanoma	Distant Mets
FFPE-24	NRAS_Q61R / PIK3CA_H1047R	COSM584 / COSM775	4.8% / 24.7%	N / Y	3.1	Breast	Primary
FFPE-25	NRAS_G12D	COSM564	38.3%	Y / Y	4.4	Melanoma	Primary
FFPE-26	NRAS_G12C	COSM562	9.7%	Y	5.8	Brain	Primary
FFPE-27	EGFR_T790M	COSM6240	29.8%	Y	2.2	Breast	Distant Mets
FFPE-28	EGFR_G719A	COSM6239	10.4%	Y	5.9	Brain	Primary
FFPE-29	PTEN_R233	COSM5154	7.3%	Y	6.3	Sarcoma	Primary
FFPE-30	PTEN_Q245	COSM5159	6.7%	Y	4.5	Brain	Primary
FFPE-31	KRAS_Q61H	COSM554	4.9%	Y	5	Appendiceal	Distant Mets
FFPE-32	KRAS_Q61L	COSM553	50.6%	Y	2.4	Colorectal	Primary
FFPE-33	KRAS_G12A	COSM522	14.0%	Y	4.2	Breast	Distant Mets
FFPE-34	KRAS_G12C	COSM516	13.3%	Y	3.9	Colorectal	Primary
FFPE-35	KRAS_G12D	COSM521	5.4%	Y	5.4	Appendiceal	Primary
FFPE-36	KRAS_G12R	COSM518	7.8%	Y	4.1	Lung	Primary
FFPE-37	KRAS_G12S	COSM517	8.5%	Y	3.7	Colorectal	Primary
FFPE-38	KRAS_G12V	COSM520	5.0%	Y	5.5	Pancreatic	Primary
FFPE-39	KRAS_G12D	COSM532	7.7%	Y	4.6	Colorectal	Distant Mets
FFPE-40	PIK3CA_H1047R	COSM775	6.7%	Y	6.2	Head and Neck	Primary
FFPE-41	PIK3CA_E545Q	COSM27133	12.4%	Y	4.9	Colorectal	Primary
FFPE-42	PIK3CA_E542K	COSM760	9.7%	Y	5	Sarcoma	Primary
FFPE-43	PIK3CA_Q546R / KRAS_G12D	COSM12459 / COSM521	16.7% / 32.6%	Y / Y	2.6	Colorectal	Primary
FFPE-44	PIK3CA_E545K	COSM763	4.8%	Y	6.2	Brain	Primary
FFPE-45	NRAS_G12D / BRAF_D594G	COSM564 / COSM467	38.8% / 10.2%	Y / Y	4.4	Melanoma	Primary
FFPE-46	FBXW7_R465C / EGFR_L747_S752delIREATS	COSM22932 / COSM12382	8% / 2.4%	Y / Y	2.7	Bladder	Met

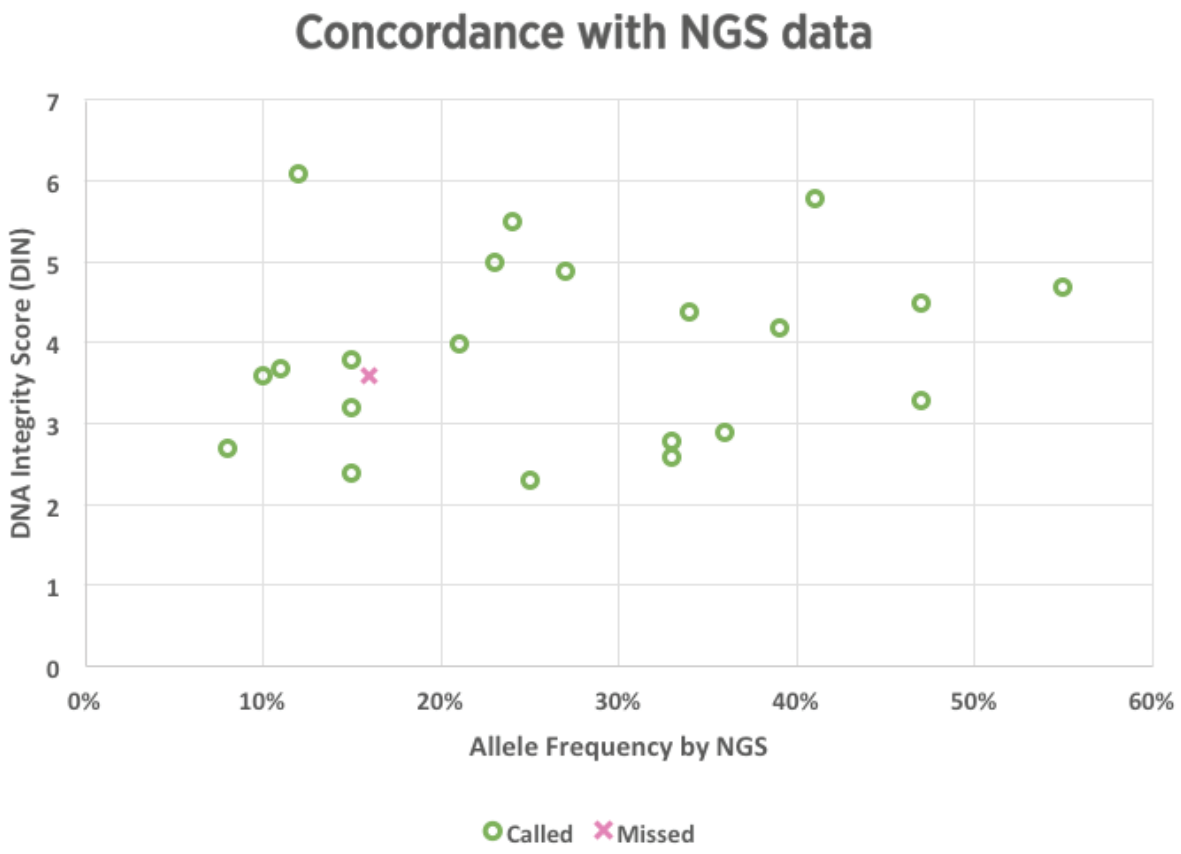
High Concordance with NGS Data

Table 2: Variant detection and identification concordance between Next-Generation Sequencing and the Vantage 3D DNA SNV Panel

		Vantage 3D DNA SNV Panel	
		Detected	Undetected
Next-Gen Sequencing	Detected	53	1
	Undetected	1	3,159

Table 3: Summary statistics for Vantage 3D DNA SNV Panel with reference to NGS data

Sensitivity	Specificity	Precision	Accuracy	FDR
98.1%	100.0%	98.1%	99.9%	1.9%



Above: Over a range of sample qualities and allele frequencies, FFPE-derived gDNA from MD Anderson samples and commercially obtained FFPE specimens assayed with the Vantage 3D DNA SNV Panel yielded high concordance with Next-Generation Sequencing.

Ordering Information:

Description	Format	Quantity	Catalog Number
nCounter Vantage 3D DNA SNV Solid Tumor Panel	Code Set Only; Includes Reagents for Pre-amp	12 reactions	VDXC-HST-12
nCounter Master Kit (Max or FLEX Systems)	Reagents and Cartridges	12 reactions	NAA-AKIT-012

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