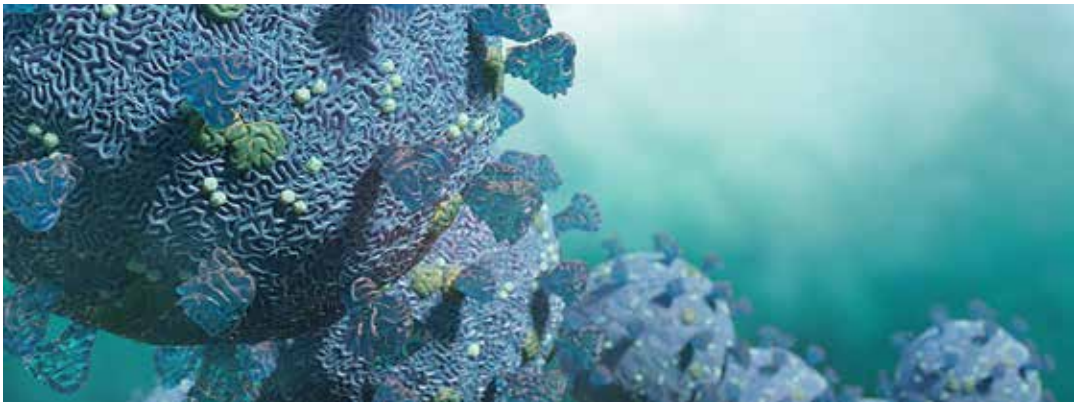
Genexus System news

Issue: October 2020

See what's happened over the past few months



New assays available on the Genexus System

- The Ion AmpliSeq™ SARS-CoV-2 Research Panel, one assay surveying the entire coronavirus genome for epidemiological investigation, is now available on the Ion Torrent™ Genexus™ System. You will hear more about this assay in the next issue of Genexus System news.
- The Ion Torrent™ Oncomine™ Myeloid GX Assay is also available on the Genexus System.Read more about this on last page.

GlobalAccess Sequencing Program launch and extension

Earlier this year Thermo Fisher Scientific launched the GlobalAccess Sequencing Program to accelerate multi-institutional studies focused on SARS-CoV-2, and this month we announced its expansion to include laboratories working in oncology. The expanded program provides support to labs facing significant hurdles as a result of the global pandemic by offering faster access to comprehensive, single-day molecular profiling of tumor tissue on the Genexus System. Get significantly subsidized access to the Genexus System now.

First step on our journey to democratize NGS-based CDx

The United States Food and Drug Administration (US FDA) has granted Breakthrough Device Designation to the Oncomine™ Precision Assay to identify low-grade glioma (LGG) patients with isocitrate dehydrogenase 1 and 2 (*IDH1* and *IDH2*) mutations who may be eligible for vorasidenib (AG-881), currently in an investigational phase 3 INDIGO study.

This is the first important milestone on our journey to gaining regulatory approval for the Oncomine Precision Assay, a next-generation companion diagnostics (CDx) solution. Read more.

“ Quote of the month

“We know that the COVID-19 pandemic has interrupted the way laboratories function on a daily basis. For some, it has deeply impacted their ability to serve customers in circumstances where time is of the essence. At this unprecedented time, sustaining the momentum in oncology is paramount. Extending the benefits of GlobalAccess to this community is a natural extension of our mission to enable our customers to help make the world healthier, cleaner and safer.”

–Garret Hampton, president of clinical next-generation sequencing and oncology at Thermo Fisher Scientific

ThermoFisher SCIENTIFIC

Four Genexus System customers shared their experience during the virtual OncomineWorld conference

Four users of the Genexus System evaluated it using Oncomine assays and found that:

- Molecular diagnostics is becoming progressively more demanding
- Flexible adaptation to the needs of the market is very important, and increasing complexity requires solutions to minimize the workload
- The Genexus System is a potential future solution combining all steps of diagnostic NGS

Sample type	Variant type	Sensitivity	Specificity	Concordance
FFPE	Indels	100%	100%	100%
	SNVs	94%	100%	94%
	SNVs and indels	95%	100%	95%
	CNVs	100%	100%	100%
	Fusions	96%	100%	96%
Plasma	Indels	95%	100%	95%
	SNVs	100%	100%	100%
	SNVs and indels	95%	100%	95%
	CNVs	100%	100%	100%

Presented by Michael Hummel at OncomineWorld May 14, 2020

Michael Hummel, PhD

Head of Molecular Pathology, Charité—Universitätsmedizin Berlin, Institute of Pathology

Evaluated Genexus System using the Oncomine Precision Assay with cytology smear samples:

- Smear samples are fixated in alcohol; more than 50% of them have <20% tumor cells by laser capture microdissection
- Previously NGS analysis was performed after enrichment by laser capture microdissection

The Oncomine Precision Assay was able to detect all alteration without any enrichment:

- Included molecular tagging increases sensitivity and specificity
- Previously identified alterations were detected in samples with cellularity of 5% and a very low allelic frequency (AF) around 2%, with no false positives
- In a dilution experiment all previously detected alternations were detected down to 1:32 dilution, down to an AF of 1%, with no false positives

Sample ID	%TCC	Variant	AF (LCM)	AF (Oncomine)
8141	10	EGFRpL858R	18%	2.2%
8360	10	EGFR p.E746_A750del	70%	17%
8756	5	KRAS p.G12C	61%	2.1%

Philip Jermann, PhD

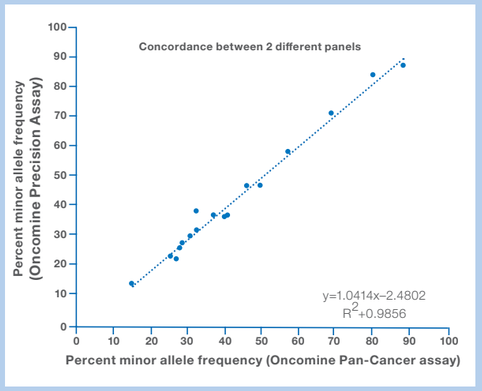
Director of the Molecular Assay Development Unit, Institute of Pathology and Medical Genetics of Basel

Evaluated the Oncomine Precision Assay on liquid biopsy samples and highlighted the following benefits addressing the biggest barriers for broad NGS implementation so far:

- Fully automated and highly accurate NGS system
- 1-day turnaround time
- No batching required

Results from liquid biopsy sample analysis:

- Hotspot mutations, copy number variants (gains and losses), and fusion drivers were detected in control tissues and cell-free total nucleic acid (TNA) using Oncomine Precision Assay
- Sensitizing *EGFR* mutations detected from 14 *EGFR*-positive plasma samples were in complete concordance with tissue samples
- Concordance with the Ion Torrent™ Oncomine™ Pan-Cancer cfDNA assay was >98%



Siew-Kee (Amanda) Low, PhD

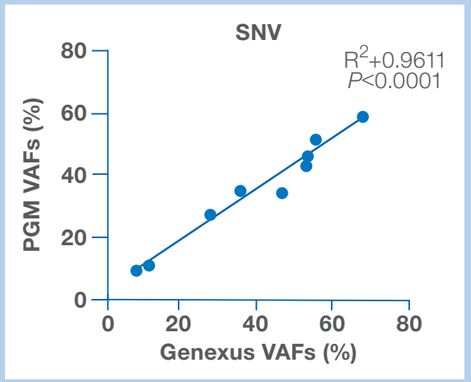
Group Leader for Cancer Neoantigen Vaccine Development Group, Cancer Precision Medicine Center, Japanese Foundation for Cancer Research (JFCR)

Evaluated the Genexus System using the Oncomine Comprehensive Assay and highlighted the following benefits:

- Single touchpoint—total hands-on time of 10 minutes
- 27 hours from nucleic acid to result
- Multiplex capability—up to 32 library preparations per run
- 2 week on-instrument chip and reagent stability—flexibility in batch size

Comparison with analysis of same samples on Ion PGM™ system

- N = 24 samples (12 DNA, 12 RNA)
- Somatic aberrations
  - SNVs/indels [n=11]
  - CNVs [n=6]
  - Gene fusions [n=12]
- Concordance across aberration type: 100%



Kojo Elenitoba-Johnson, MD

Director, Center for Personalized Diagnostics Director, Division of Precision and Computational Diagnostics, University of Pennsylvania Perelman School of Medicine

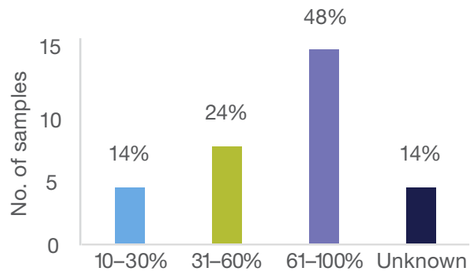
Full results of the multi-center study for evaluation of the Genexus System and Oncomine Precision Assay

Presented at OncomineWorld on May 14, 2020

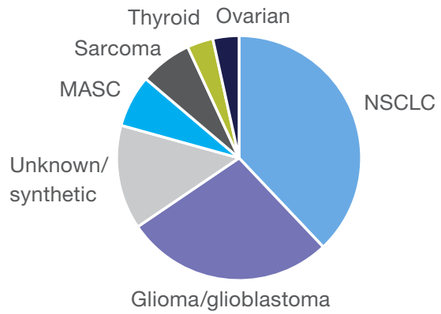
Study overview:

- Participants: IPATIMUP, University Hospital Basel, The Charité—Universitätsmedizin Berlin, and INT Fondazione Pascale Naples
- Each participating site selected their own clinical research samples (FFPE tissue and plasma samples), of which a majority were previously characterized to have a known variant by other assays and/or technologies
- In total, 74 FFPE samples and 12 plasma samples were analyzed

FFPE samples for detection of fusions

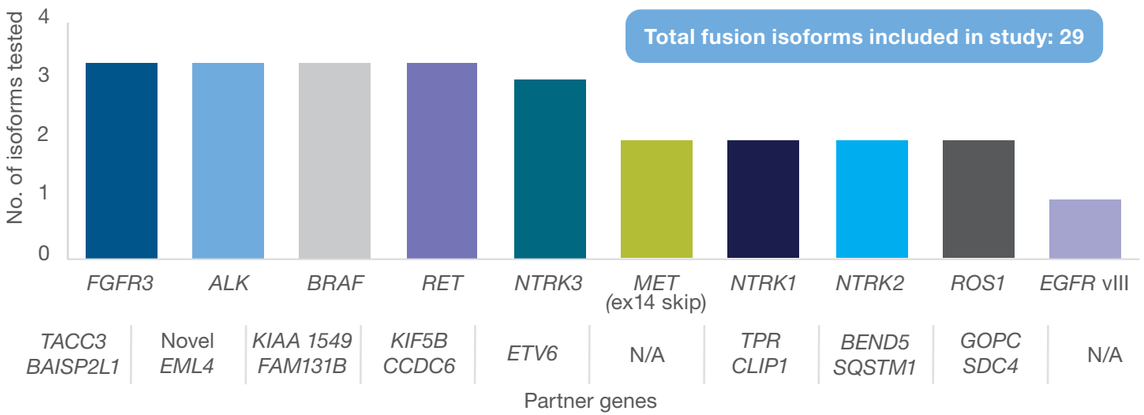


Distribution of tumor cellularity
FFPE samples used for fusion detection represented a wide range of tumor cellularity, and included the 14% of samples with under 30% tumor content.



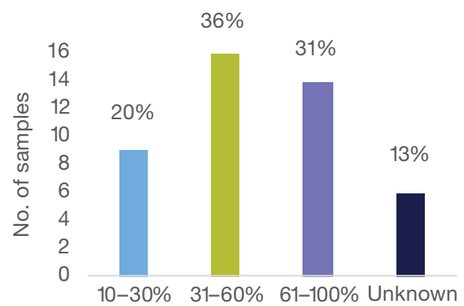
Distribution of cancer types
For assessment of fusions using FFPE, a total of 29 samples were used across a range of cancer indications, with a majority being NSCLC, followed by glioma/glioblastoma.

Fusion detection in FFPE samples

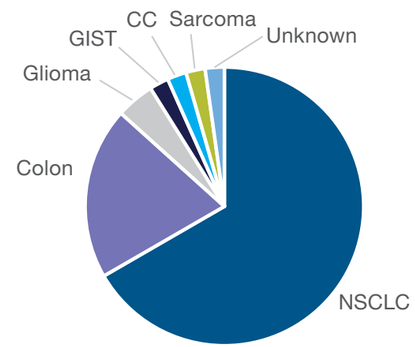


Multi-center study for evaluation of the Genexus System and Oncomine Precision Assay, presented at OncomineWorld, May 14, 2020.

FFPE samples used for detection of mutations (SNVs and indels)



Distribution of tumor cellularity
FFPE samples used for mutation detection represented a wide range of tumor cellularity; 20% of samples had under 30% tumor content.



Distribution of cancer types
For assessment of mutation detection (SNVs and indels) using FFPE, a total of 45 samples were used across a range of cancer indications, with a majority being NSCLC.

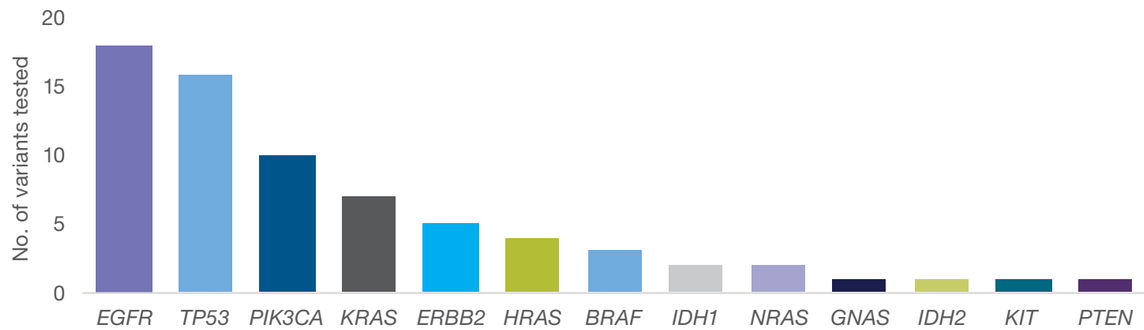
Detection of typical variants in relevant genes

EGFR mutations	Count
EGFR p.L858R	8
EGFR p.E746_A750del	6
EGFR p.S768_D770dup	2
EGFR p.747_P753delinsS	1
EGFR p.T790M	1

PIK3CA mutations	Count
PIK3CA p.E542K	6
PIK3CA p.E545K	1
PIK3CA p.G1049R	1
PIK3CA p.H1047L	1
PIK3CA p.H1047R	1

KRAS mutations	Count
KRAS p.G12C	4
KRAS p.G13D	1
KRAS p.A146T	1

ERBB2 mutations	Count
ERBB2 p.V8421	3
ERBB2 p.G776delinsVC	1
ERBB2 p.V772_A775dup	1

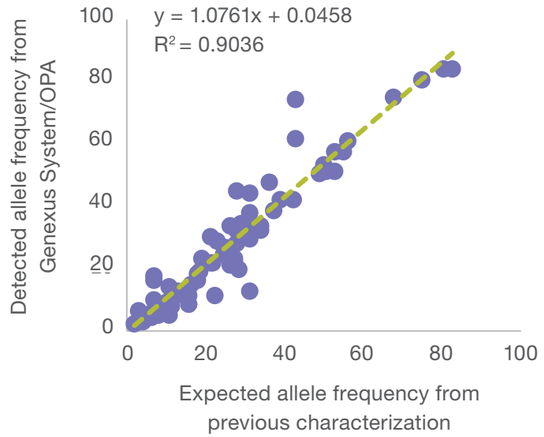


Multi-center study for evaluation of the Genexus System and Oncomine Precision Assay, presented at OncomineWorld, May 14, 2020.

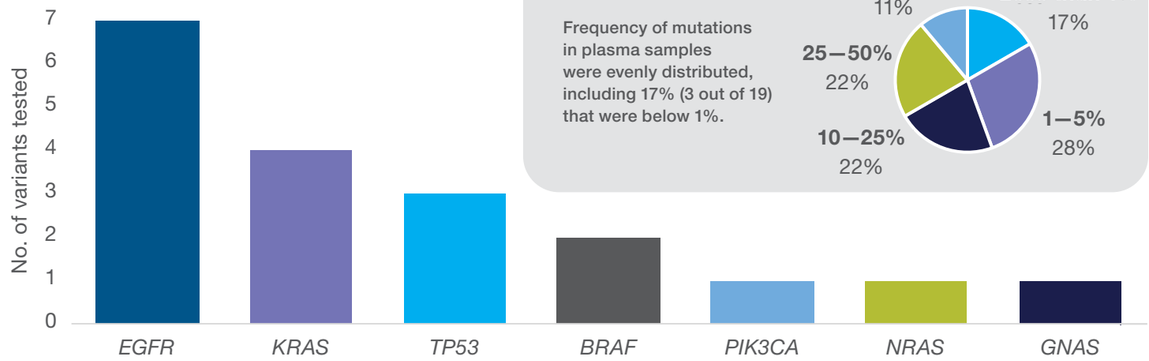
Comparison with other technologies

Variant type	Sensitivity	Specificity	Concordance
Indels	100%	100%	100%
SNVs	94%	100%	94%
SNVs and indels	95%	100%	95%

- When compared with the previous characterization, the performance (sensitivity, specificity, and concordance) of mutation detection in FFPE samples was high using **the Genexus System and Oncomine Precision Assay**
- Additionally, the correlation in measurement of **allele frequency** was also high, with an R^2 of 0.9036
- Previous characterization included the Ion Torrent™ Oncomine™ Focus Assay, Oncomine™ Solid Tumor kits, Ion AmpliSeq™ Colon and Lung Cancer Research Panel v2, and Illumina™ TruSight™ Tumor 170 Kit

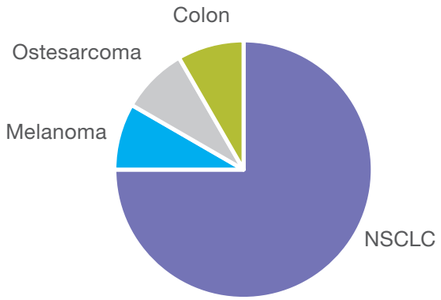


Liquid biopsies: Distribution of mutations

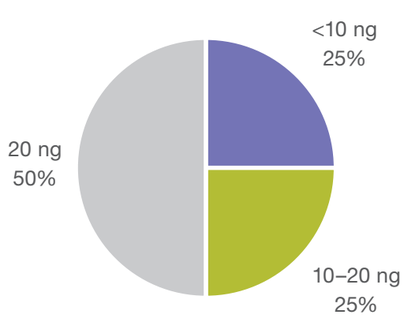


Frequency of mutations in plasma samples were evenly distributed, including 17% (3 out of 19) that were below 1%.

Liquid biopsies: Cancer types investigated and tumor cell content



Distribution of cancer types
For assessment of mutations using plasma, a total of 12 samples were used across a range of cancer indications, with a majority being NSCLC.



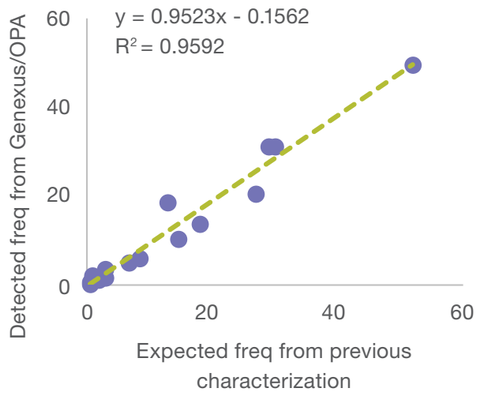
cfTNA input range
50% of the plasma samples were successfully sequenced using less than the recommended 20 ng of cfTNA input.

Multi-center study for evaluation of the Genexus System and Oncomine Precision Assay, presented at OncomineWorld, May 14, 2020.

Liquid biopsies: High concordance with existing data

Variant type	Sensitivity	Specificity	Concordance
Indels	95%	100%	95%
SNVs	100%	100%	100%
SNVs and indels	95%	100%	95%
CNVs	100%	100%	100%

- Previous characterization included: Ion Torrent™ Oncomine™ Pan-Cancer Cell-Free Assay and Ion Torrent™ Oncomine™ Cell-Free Total Nucleic Acid Research Assay
- Results above included a concordant detection of a *FGFR1* amplification from a colorectal cancer sample
- Additionally, the correlation in measurement of allele frequency was also high, with an R^2 of 0.9592



Study results summary:

- Results from this study demonstrated that the Genexus System and the Oncomine Precision Assay **can properly detect different variant types in both FFPE and plasma samples**
- Implementation and operation of the Genexus System and the Oncomine Precision Assay was **successful across four external customer sites** with a variety of banked cancer samples
- Comparison to previous characterization demonstrated **high performance for all variant and sample types**

Multi-center study for evaluation of the Genexus System and Oncomine Precision Assay, presented at OncomineWorld, May 14, 2020.

Introducing the Oncomine Myeloid Assay GX

One-day genomic profiling for myeloid samples

Myeloid samples can be challenging to profile. They're complex and heterogeneous, and they can proliferate rapidly. Traditional single-gene approaches to myeloid profiling can be laborious and time-consuming—especially as the list of relevant genes continues to grow. Laboratories need a streamlined way to profile all key mutations, quickly and efficiently.

Now there is a better solution. With the Ion Torrent™ Oncomine™ Myeloid Assay GX on the Genexus System, you can get a comprehensive myeloid mutational profile from a single NGS run, with results in just one day.*

A highly integrated workflow lets you go from specimen to report with only 10 minutes of hands-on time and two user touchpoints. It's never been easier to implement NGS testing in your lab.

With the Oncomine Myeloid Assay GX, you can profile 40 DNA target genes and 29 RNA fusion driver genes simultaneously. This broad fusion panel allows you to detect over 600 unique fusion isotypes. The panel content is applicable to all the major myeloid disorders—AML, MDS, MPN, CMML, and JMML.

***The Pathologist* webinar: A new day for myeloid genomic profiling: how NGS advancements are providing deeper insight with faster time to results**

View on demand on www.oncomine.com/myeloid

Dr. Kojo Elenitoba-Johnson

- Professor. University of Pennsylvania Perelman School of Medicine
- Director, Center for Personalized Diagnostics
- Director, Division of Precision and Computational Diagnostics

Dr. Andy Felton

- Vice President of Product Management, Clinical Next-Generation Sequencing, Thermo Fisher Scientific

View on demand

Find out more about the Genexus System and the available assays at **oncomine.com** and **thermofisher.com/newday**

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