NEO
GENOMICS

Multiplexed Immuno-fluorescence

MultiOmyx™ and Akoya
PhenoImager™ platforms

13 Global Locations
across 2 continents

>1,500
completed projects with a backlog of more than $250MM

>100
CDx programs

#1
in PD-L1 Testing and breast cancer * testing
*Data from CMS claims database

>120
MDs and PhDs across pathology and scientific disciplines

~1,000,000
cancer-related lab tests per year

550+
oncology and pathology tests ready for order

Our mission:
Transforming care for cancer patients

Because every sixth death in the world is due to cancer, our mission at NeoGenomics is to partner with pharmaceutical companies to bring new life-saving oncology drugs to market so we can help reduce cancer-related deaths worldwide.

Our unique and comprehensive product and service offerings include:

- Unparalleled expertise, flexibility and scalability
- Largest oncology focused clinical research organization (CRO) in the USA
- One unified lab with comprehensive services
- Medical and scientific consultation

Multiplexed immunofluorescence

A complete view of tumor behavior

Utilizing deep learning and advanced cell classification algorithms, multiplexed immunofluorescence (IF) spatial analysis uncovers the complex interplay between multitudes of immuno-oncology biomarkers, and provides complete analysis of the tumor microenvironment.

Multiplexed immunofluorescence has emerged as an effective and proficient approach to simultaneously identify specific proteins and immune cell types, to determine the spatial distribution and activation state of immune cells, as well as the expression of immune modulators, all at the same time. This method is highly beneficial for exploring immune evasion mechanisms and finding potential biomarkers that allow researchers to assess the mechanism of action and predict and monitor drug response.

NeoGenomics' Pharma Services offers two multiplexed immunofluorescence platforms:

MultiOmyx™

MultiOmyx is a proprietary, high-order multiplexing methodology that enables visualization and characterization of up to 60 proteins in a single FFPE tissue section.

- High order ≥ 7plex
- Comprehensive analysis of tumor biology
- Deep and precise immuno-profiling

PhenoImager™ HT

PhenoImager HT is an automated system that allows simultaneous detection of 2-6 different markers from a single FFPE tissue slide which would provide a streamlined workflow for implementing refined low-order multiplex panel sets.

- Low order 2—6plex
- High-throughput and faster TAT
- Assay transfer and validation

MultiOmyx

## Proprietary, high-order, multiplexing methodology

MultiOmyx (MO) enables visualization and characterization of up to 60 proteins in a single formalin-fixed, paraffin-embedded (FFPE) 4µm tissue section. Slides are prepared and stained using MultiOmyx multiplexing IF staining protocol. For each round of staining, conjugated fluorescent antibodies are applied to the slide, followed by image acquisition of stained slides. The dye is erased, enabling a subsequent round of staining with another pair of fluorescent antibodies.

MultiOmyx also offers:

- Unambiguous immune cell co-expression and co-localization
- Advanced quantitative cellular classification
- Medical, scientific, and bioinformatics consultation
- Custom assay design and verification
- Advanced image analysis and visualization tools
- Spatial analytics
- Integrated with FISH, RNAScope, and NGS

- High order: >= 7-plex
- Comprehensive analysis of tumor biology
- Monitoring of the immune microenvironment for the characterization of tumors pre- and post- I/O treatment
- Comprehensive Immunophenotyping at single cell level from one FFPE slide
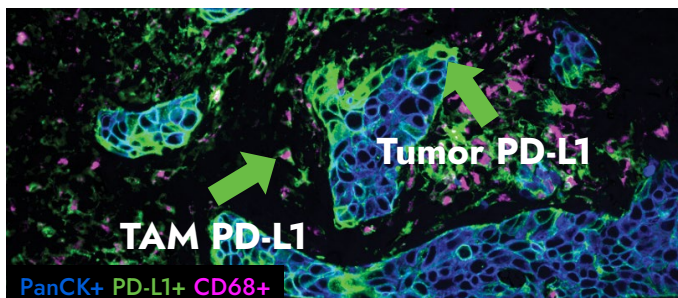
## MultiOmyx overlay images — NSCLC sample multiplexed with a 16-marker panel
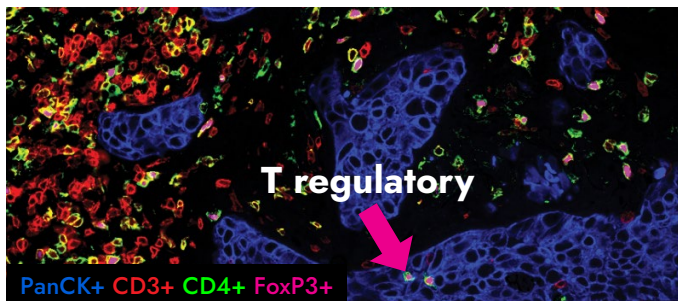
T helper cells co-expressing CD3 and CD4 are yellow, and the arrow indicates a T regulatory cell with a magenta nuclear stain.
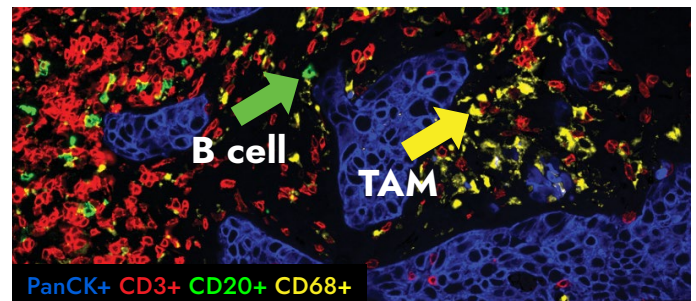
B cells expressing CD20 are green, and tumor associated macrophages (TAMs) expressing CD68 are yellow.

The two arrows indicate examples of a tumor associated macrophage (TAM) positive for PD-L1, versus a tumor cell positive for PD-L1.
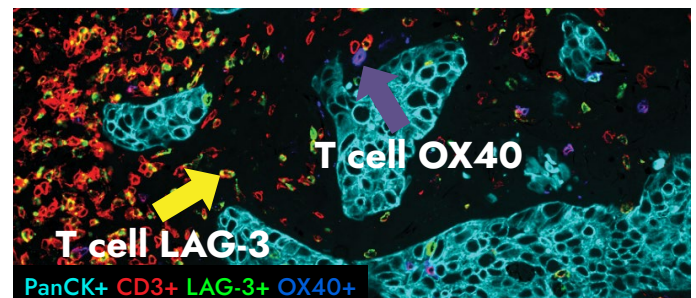

CD3-positive T cells expressing LAG-3 are yellow, while T cells expressing OX40 are magenta.

Verified panels

Customization and more verified panels available

Immune panel (TIL) — 12 markers

| BIOMARKER	CO-EXPRESSION	PHENOTYPES
CD3	CD3+CD4+	T helper
CD4	CD3+CD4+FoxP3+	T regulatory
CD8	CD3+CD4+CD45RO+	Memory T helper
CD45RO	CD3+CD4+PD1+	Immune modulation
FoxP3	CD3+CD4+CTLA4+	Immune modulation
CD20	CD3+CD8+	T cytotoxic
CD68	CD3+CD8+CD45RO+	Memory T cytotoxic
CD56	CD3+CD8+PD1+	Immune modulation
CTLA-4	CD68+PDL1+	Macrophage PD-L1
PD-1	CD20+PDL1+	B cell PD-L1
PD-L1	CD3-CD56+	Natural Killer cell
PanCK	PanCK+PDL1+	Tumor cell PD-L1

PanCK+ CD8+ PD-L1+ CD68+ FoxP3+
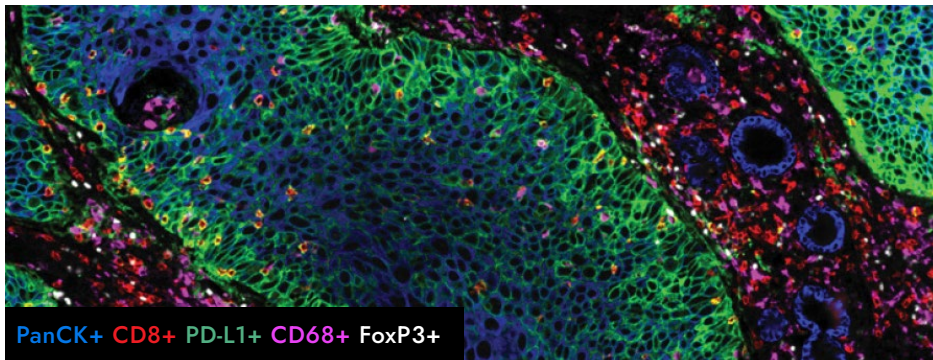
Au Q. et al. (2016). MultiOmyx™ multiplexed tumor infiltrating lymphocyte panel provides comprehensive immunophenotyping from a single FFPE slide. Poster presented at AACR Annual Meeting, New Orleans, LA.

TIL and Myeloid panel — 19 markers

| TIL & MYELOID PANEL	CO-EXPRESSION	PHENOTYPES
CD3	CD3+CD4+	T helper
CD4	CD3+CD4+FoxP3+	T regulatory
CD8	CD3+CD4+PD1+	Immune modulation
CD45RO	CD3+CD8+	T cytotoxic
FoxP3	CD8+PD1+	Immune modulation
CD11b	CD8+GranzymeB+	Effector T cytotoxic
CD14	CD3+CD45RO	Memory T cells
CD15	CD68+	TAM
CD16	CD68+MHC-II+CD163-	M1 TAM
CD33	CD68+MHC-II-CD163+	M2 TAM
CD68	CD68+PDL1+	Macrophage PD-L1
CD163	CD11b+CD33+MHC-II-	MDSC
MHC-II	CD11b+CD33+MHC-II-CD14+CD15-	M-MDSC
Arginase1	CD11b+CD33+MHC-II-CD14-CD15+	G-MDSC
GranzymeB	PanCK+Ki67+	Proliferating tumor
Ki67	PanCK+PD-L1+	Tumor cell PD-L1
PD-1		
PD-L1		
PanCK		

PanCK+ CD11b+ CD3+ CD15+ FoxP3+
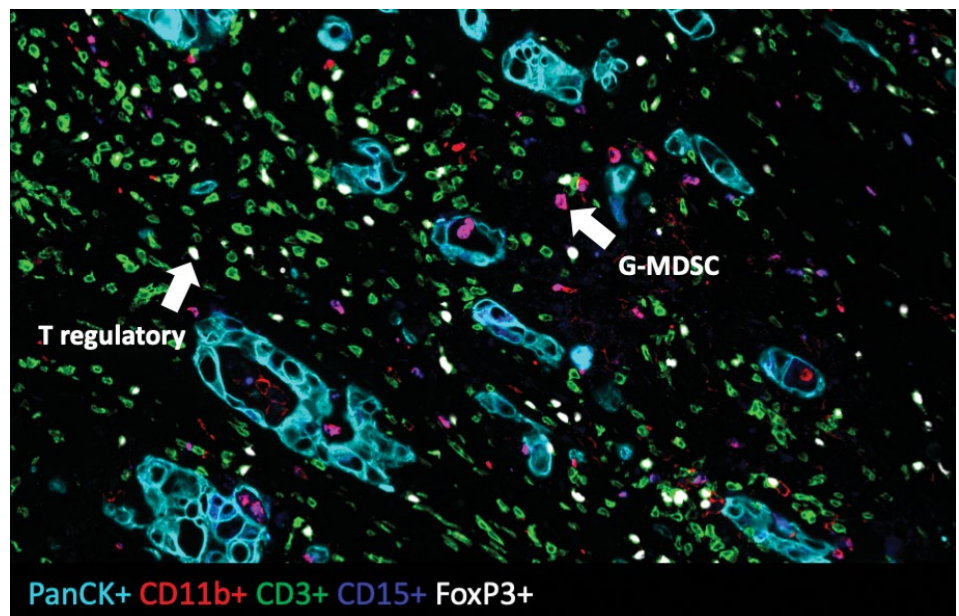
Juncker-Jensen A. et al. (2018). Using MultiOmyx™ to Analyze Correlations between Immunosuppressive Cells and Tumor-Infiltrating Lymphocytes in the Pancreatic Tumor Microenvironment. Poster presented at ESMO Annual Meeting, Munich, Germany.

NeoVUE™

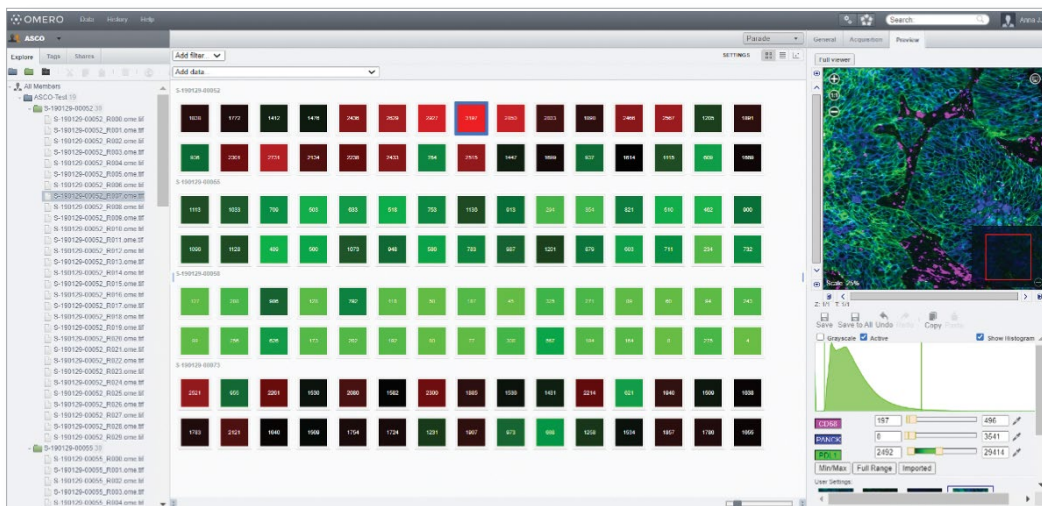## Image and data visualization software

With the NeoVUE image and data visualization software the MultiOmyx end-user can rapidly view and manage the multiplexed images as well as the comprehensive biomarker profiling on a single-cell level.

Image visualization
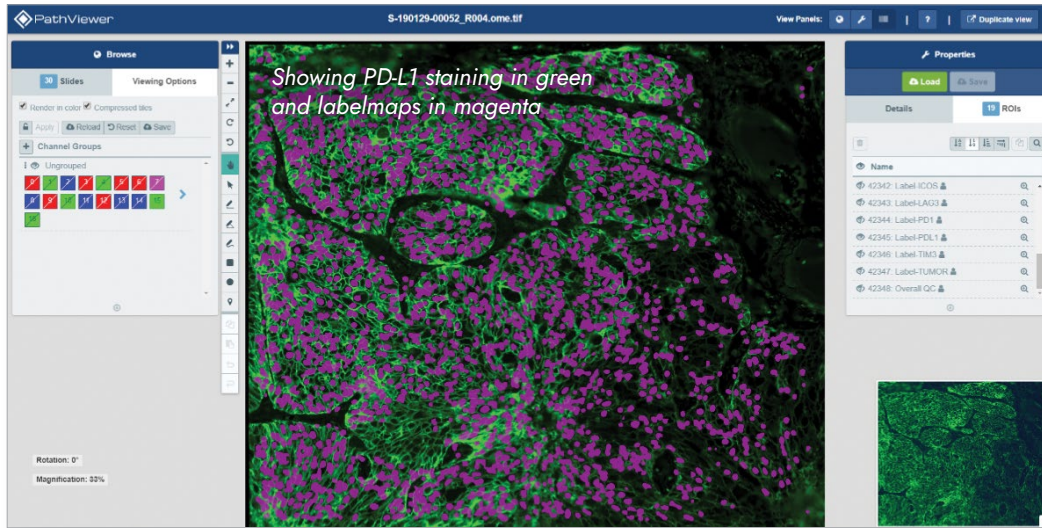
MultiOmyx images can be viewed via NeoVUE in a web browser remotely on Windows, macOS or Linux and it supports panning, zooming, and rotation of large images. This software complements the data output and images generated with MultiOmyx, and contains intuitive point-and-click visualization of IF images, classification label maps, tumor segmentation masks, and color blends.

Data visualization

In addition to supporting image visualization, NeoVUE software also enables the user to interrogate study data via scatter plots, heat maps and filters for quantitative cell counts or densities, of single markers or co-expressions. In this example a heat map was generated based on the number of cells positive for PD-L1 in each region of interest, across all samples multiplexed.

PhenoImager™

High throughput automated multispectral imaging

PhenoImager HT is a fully-enclosed instrument with touchless slide automation that allows simultaneous detection of 2-6 different markers from a single FFPE tissue slide—providing a streamlined staining, imaging and analysis workflow for implementing optimized low-order multiplex panel sets.

PhenoImager HT offers:

- Whole slide multispectral images at high throughput with up to 6 markers
- Assay transfer and validation
- Continuous slide loading workflows (80+ slides)
- 6-8 slides per hour for 20x fluorescent whole slide scan
- High signal: noise ratio
- Analysis:
  — inForm®: spectrally unmixing images
  — HALO® or VisioPharm®: tissue segmentation, cell segmentation, phenotyping, scoring, spatial distribution analysis, pathology views
- Custom panels also available
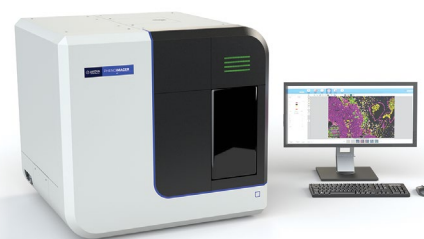
Whole slide imaging system

IMMUNE CELL PANEL #1	IMMUNE CELL PANEL #2	IMMUNE CELL PANEL #3	IMMUNE CELL PANEL #4
CD3	CD3	CD8	CD19
CD4	CD163	FoxP3	CD68
CD8	MHC-II	PD-1	CD56
FoxP3	CD68	CD68	MHC-II
CD68	CD56	PD-L1	PD-L1
PanCK	CD20	PanCK/SOX10	PanCK

T CELL PANEL #1	T CELL PANEL #2	T CELL PANEL #3	T CELL PANEL #4
CD3	CD4	CD3	CD3
CD4	CD8	CD4	CD4
CD8	PD-1	CD8	CD8
CD45RO	LAG3	FoxP3	FoxP3
FOXP3	TIGIT	PD-1	PanCK
PanCK		PanCK	

Data image analysis

Indica HALO®

- User-friendly UI and Custom Development Workflow
- Library of pre-configured modules available
- HALO Link allows slide review and direct annotation by pathologists
- Better fit for clinical trials because of the nature of the quality/regulatory requirements
- Marketing partnership with NeoGenomics
- Generates results very quickly for common tasks/ simple analytics/single-plex
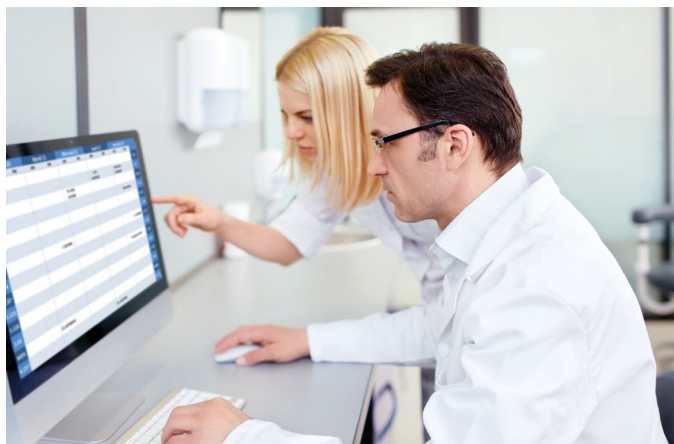
VisioPharm®

- Library of prebuilt apps available
- Powerful tool set, optimal for more complex and custom analytics requirements
- Can define non-cell objects in the tissue
- AI packages can be used for cell classification to increase accuracy
- Clinical trial testing is feasible but requires more time and effort

NeoLYTX

- AI-based framework proprietary to NeoGenomics
- Optimized for MultiOmyx
- Highly customizable with complete control to accommodate new requirements
- Adapted for IHC/CISH/dual IHC
- NeoVUE compatible
- RUO (software not validated to FDA standards)

PLATFORM	INDICA HALO	VISIOPHARM	NEOLYTX
Currently Supporting Clinical Studies (retro)	+++	++	+++
Clinical Studies (enrollment)	++	+	N/A
Low order mIF, 2-6-plex (PhenoImager)	+++	+++	++
High-plex mIF, ≥7 (MO)	N/A	N/A	+++
Complexity of analytics tasks	+	++	+++
Direct annotation and slide review	+++	+++	N/A
Defining non-cell objects	N/A	++	+++

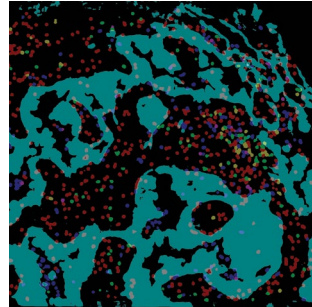# General Data Image Analysis Workflow

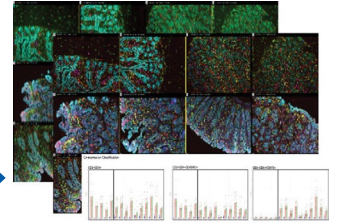**Single section for all biomarkers**

IF overlay image
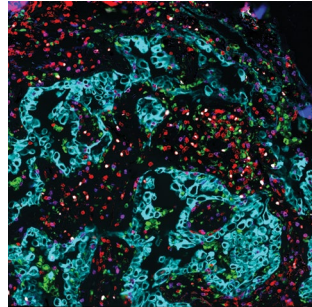
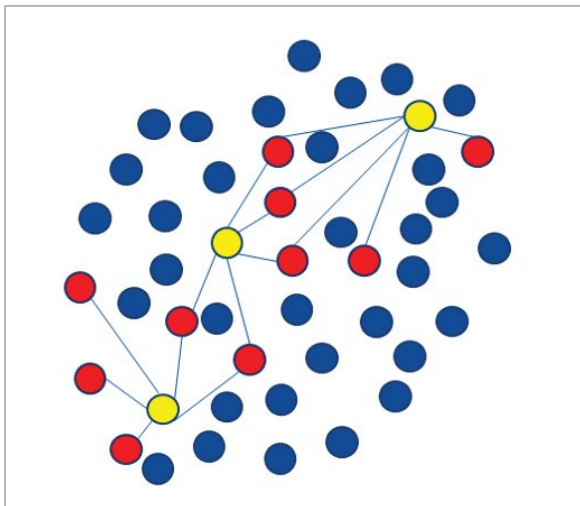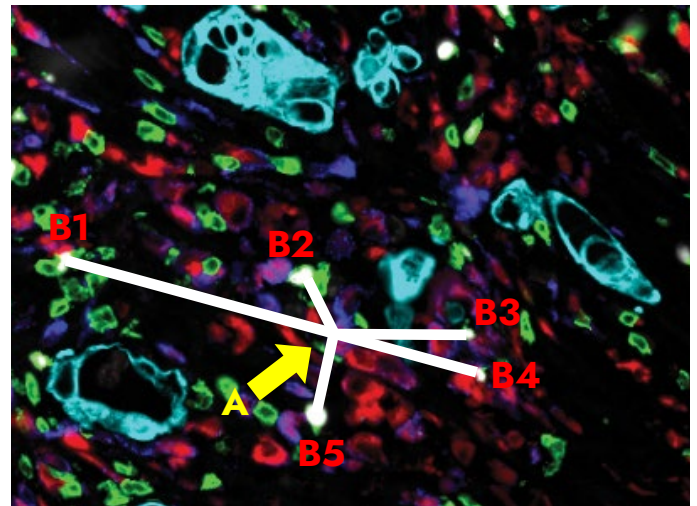**Cell and region classification**

Data interrogation

MultiOmyx™ Spatial Analytics: Nearest Neighbor Analysis

The average of the distance to the 5 nearest neighbors from any given phenotype is calculated

⬤ (yellow) Phenotype A
⬤ (red) Phenotype B

The relationship between a cell and its 5 nearest Treg neighbor cells is shown as an example

B1 B2 B3 B4 B5 A

NeoGenomics is the leading global provider of oncology testing and research services, with 13 locations across 2 continents.

#	Location
1	Fort Myers, Florida (*Est. 2002*) *Headquarters*
2	Aliso Viejo, California (*Est. 2004*)
3	Atlanta, Georgia (*Est. 2017*)
4	Cambridge, UK (*Est. 2014*)
5	Carlsbad, California (*Est. 2004*)
6	Chicago, Illinois (Est. 2022)
7	Fresno, California (*Est. 2014*)
8	Houston, Texas (*Est. 2001*)
9	La Jolla, California (*Est. 2014*)
10	Nashville, Tennessee (*Est. 2006*)
11	Phoenix, Arizona (*Est. 2021*)
12	RTP, North Carolina (*Est. 2016*)
13	Tampa, Florida (*Est. 2011*)

About NeoGenomics Pharma Services

NeoGenomics' Pharma Services unifies several innovative companies' scientific and medical leadership under one leading brand, offering one of the most comprehensive laboratory services menu available for biomarker testing supporting oncology clinical trials globally. We provide our clients with an unparalleled level of expertise, service, flexibility, and scalability. Additionally, we offer alternative business models and solutions across the continuum of development from pre-clinical research and development through commercialization.

To learn more about NeoGenomics Pharma Services, visit us online at neogenomics.com/pharma-services, call us at 800.720.4363 or email us at pharmaservices@neogenomics.com

NeoGenomics Laboratories is a specialized oncology reference laboratory providing the latest technologies, testing, partnership opportunities, and interactive education to the oncology and pathology communities. We offer the complete spectrum of diagnostic services through our nationwide network of CAP-accredited, CLIA-certified laboratories.

Committed to research as the means to improve patient care, we provide Pharma Services for pharmaceutical companies, in vitro diagnostic manufacturers, and academic scientist-clinicians. We promote joint publications with our client physicians. NeoGenomics welcomes your inquiries for collaborations. Please contact us for more information.

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