

Introducing the Next Generation of Mantra

Quantitative Pathology Imaging and Analysis

KEY FEATURES:

- Visualize, analyze, quantify and phenotype immune cells in situ in solid tissues
- Multiplexed biomarker analysis of tumors and tumor microenvironment in situ
- Intuitive workflow optimized for the research pathologist
- Compact workstation for fluorescence and brightfield
- Pathology Views™ renders immunofluorescence images as H&E, DAB and hematoxylin
- Supports Akoya's Phenoptics™ Solution (staining, imaging and analysis)

The Mantra 2™ quantitative pathology workstation, with inForm® image analysis software, enables visualization, quantification and phenotyping of multiple types of immune cells simultaneously in intact formalin-fixed paraffin embedded (FFPE) tissue sections for cancer immunology research.

Unlike flow cytometry and next generation sequencing methods, which can only phenotype and quantify immune cells in homogenized samples, Mantra 2 generates digital images of FFPE tissue sections using multispectral imaging, preserving tissue architecture and morphology. This provides spatial information for a better understanding of the role and types of immune cells within tumor micro-environment, aiding in the research and identification

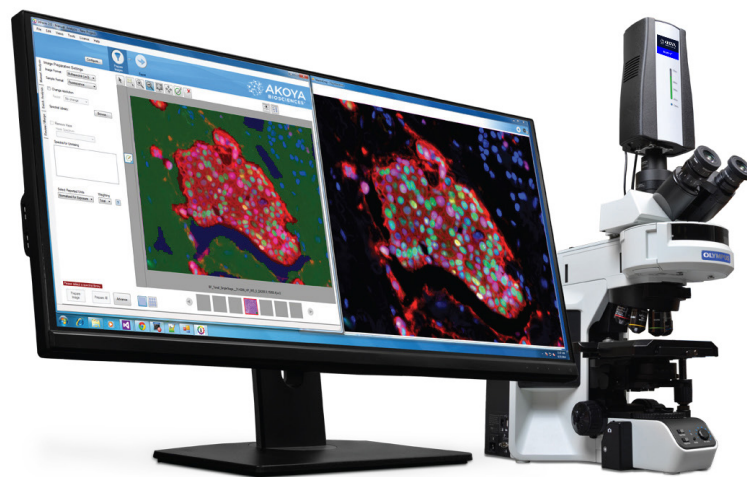
of potential cancer immunotherapy treatments.

Phenoptics™ Solutions Opal™ Multiplex IHC Kits

- Vectra® Polaris™, Vectra® 3 and
- Mantra 2™ Quantitative Pathology Imaging Systems
- inForm® Image Analysis Software
- Phenoptics Research Services

The compact Mantra 2 workstation is ideal for getting started with multispectral imaging and for assay development, freeing up higher throughput systems such as the Vectra® Polaris™ for running assays.

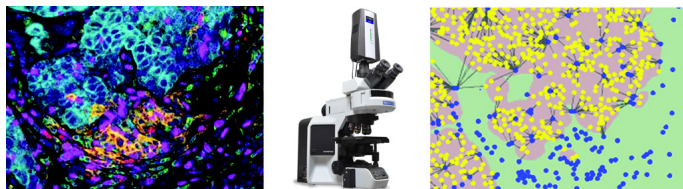
The Mantra 2 system is a part of Akoya's Phenoptics™



research solution for cancer immunology which includes staining reagents, imaging systems, and image analysis software. It comes with the inForm image acquisition and analysis software, which provides powerful tools for tissue and cell segmentation, cell phenotyping and analysis. And it can be used with a variety of stains, including Akoya's Opal™ reagent kits.

PHENOPTICS: THE COMPLETE WORK-FLOW SOLUTION

The Mantra workstation is a part of Akoya's quantitative pathology solution for cancer immunology research that includes multiplexed staining reagents and methodologies, instrumentation with unique channel-separation technology, and advanced image analysis software that can be trained to phenotype cells within the tumor micro-environment.



STAIN

Reveals Multiple Tissue Biomarkers in Context

Akoya's Phenoptics work-flow solution uses our validated and optimized Opal reagents, enabling specific staining of multiple biomarkers on a single tissue section. Opal reagents kits use sequential covalent labeling with amplification of the signal marker of interest using tyramide signal amplification (TSA), followed by removal

of the antibody. This approach has minimal impact on the overall signal and clears the tissue to be probed with another primary antibody without fear of cross-

reactivity. Users can now stain upwards of 8-markers in a single multiplex panel, allowing for greater interrogation of the tumor micro-environment and multiple pathways while retaining tissue context. This approach provides information that is not available from alternative techniques like flow cytometry or analysis of single markers in serial sections, and compatible with the standard IHC work flow in your lab. Mantra 2 can also be used with a variety of other third-party biomarker reagents to conduct multiplexed imaging.

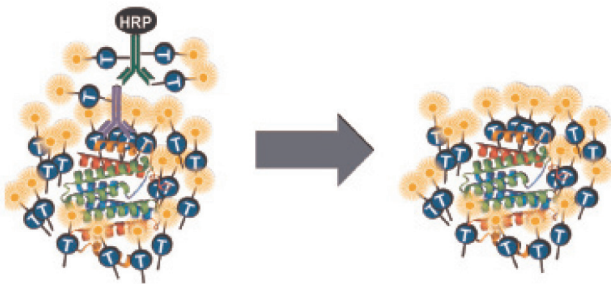


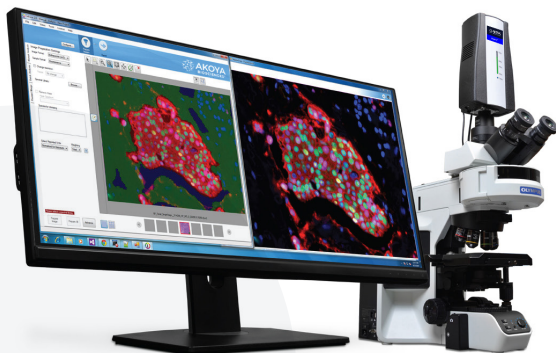
Figure 2. Opal schematic demonstrating TSA amplification (top), Breast cancer tissue using Opal reagent kits (bottom). (A) Blockade marker 1 overlaid on DAPI, (B) CD8 + signal overlaid on DAPI, (C) cytokeratin signal overlaid on DAPI, and (D) a composite image of all the markers overlaid onto DAPI. (data not shown).

IMAGE AND VISUALIZE

Visualize Immune Cells in situ

Figure 3. Mantra 2 Workstation.

The Mantra 2 workstation is an easy-to-use, compact instrument that can be used for the visualization of immune and tumor cells in situ within FFPE tissue sections. This multispectral imaging system can seamlessly transfer data, following algorithm development, from image to analysis, as well as perform automatic phenotyping. This enables immediate visualization of multiple cell types in the tumor microenvironment, thereby accelerating your research.



Features of the Mantra 2 Workstation:

- Images and spectrally separates up to eight biomarkers of interest plus autofluorescence simultaneously, enabling

more robust data quantitation to support multiplexed analysis

- Intuitive Mantra Snap™ software for integrated data transfer to inForm analysis software saving time
- Isolate autofluorescence through powerful multispectral imaging technology
- Pathology Views™ for visualization of fluorescence magery in traditional Brightfield mode (H&E, DAB and hematoxylin)
- Automated objective and filter cube changing for quicker time to data and results
- Small footprint that fits on any bench-top and allows for easy assimilation into your current work-flow
- Expanded NIR imaging range for use with dyes including Opal

Polaris 780, Alexa Fluor 750, and Cy7

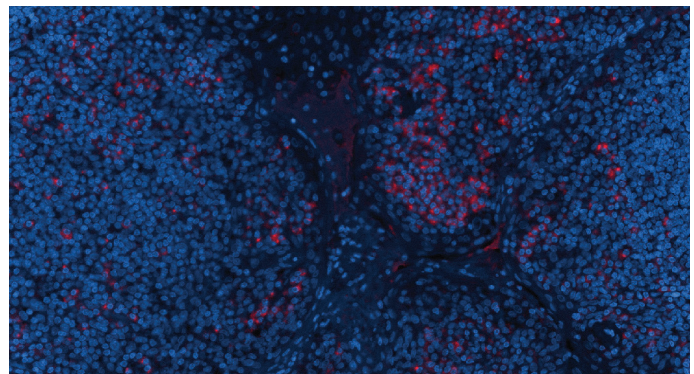


Figure 4. Tonsil stained with marker and Alexa Fluor 750 reporter dye (20x objective).

Automated Cell Detection and Segmentation

Accurately quantify biomarkers in tissue sections with inForm Tissue Finder™ automated image analysis software. Annotate regions of interest and spectrally unmix your acquired images with inForm to observe each labeled cell type. Detect and segment specific tissue types and cellular components using patented user-trainable algorithms that can recognize morphological patterns. inForm Tissue Finder includes per-cell phenotyping functionality to differentiate marked cell types (e.g. T-cells, macrophages) within a segmented area (e.g. tumor versus stroma). Features of inForm Software

- User-trained feature recognition algorithms enables automatic identification of specific tissue types based on tissue morphology
- Identify individual cell types across an entire tissue section, and within the stroma and tumor, for accurate phenotyping and spatial analysis with adaptive cell segmentation
- Quantitative per-cell phenotyping and analysis to differentiate cell types and biomarker expression in tissue sections and TMAs
- Spectrally separate fluorophore signals to reveal weakly expressing and co-localized markers
- Cellular analysis of H&E, IHC, and immunofluorescence in FFPE tissues
- Per-cell phenotyping to differentiate cell types
- Pathology Views: creates brightfield pathology (H&E, DAB and hematoxylin) renderings from the original fluorescence image
- Automatic behind-the-scenes

processing of data while Mantra 2 continues to acquire new images

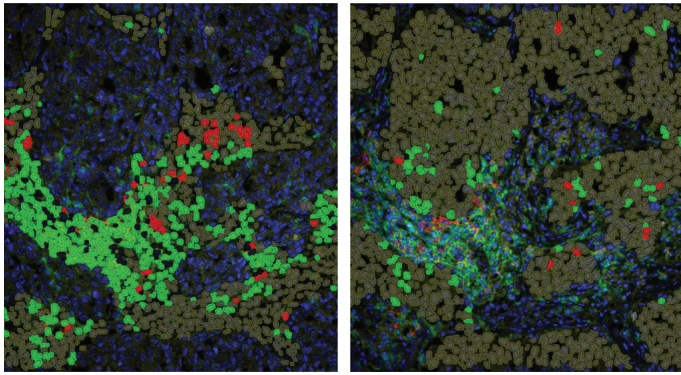


Figure 5. Helper T-cells (CD4+, green) and cytotoxic T-cells (CD8+, red) in stroma (left) and tumor (right) of breast cancer.

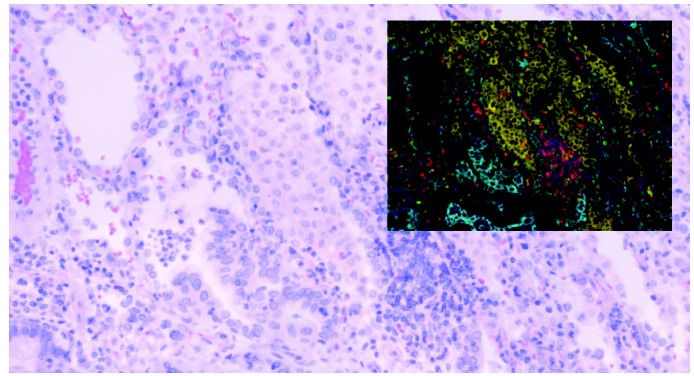


Figure 6. Pathology View rendering of original fluorescence image, seen as if it were in standard brightfield mode, providing a familiar view for a pathologist used to seeing H&E, DAB and hematoxylin.

Visualize immune cell phenotypes in the context of your tissue

Many types of immune cells play a key role in cancer tumor growth. Until recently, it was difficult to phenotype more than a couple of immune cells in solid tumors while maintaining cellular spatial relationships and morphological context. Both flow cytometry and next-gen sequencing can selectively phenotype cells in disaggregated tissues, and standard pathological analyses can deliver morphology, but without being able to analyze complex phenotypes. Akoya's Phenoptics work-flow allows for multiplexed biomarker staining, image acquisition, and data analysis, enabling multiple cell phenotypes to be studied simultaneously in solid tumors and their native micro-environment. This capability aids in the quantification of cancer-immune interactions to help researchers reveal disease mechanisms that might be in play. Together, this work-flow can help to discover and validate biomarkers, providing better data to support research into potential patient stratification methodologies.

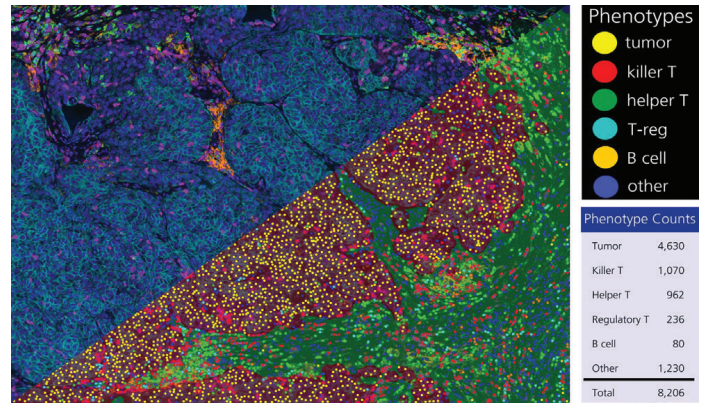


Figure 7. Breast cancer tissue showing the presence of Helper- and Cytotoxic T-cells detected within the tumor and stroma using inForm software. Upper left: Unmixed composite image with cytokeratin (cyan), Killer T-cells (purple), Helper T-cells (green), B-cells (red), PD-L1 (orange), FoxP3 (yellow), and DAPI (blue). Bottom right: Segmented tissue with cellular phenotypes displayed and quantified (chart). Work performed in collaboration with Dr. Elizabeth Mittendorf, MD, PhD, at University of Texas MD Anderson Cancer Center."

Figure 5a and 5b. The Vectra Polaris features an intuitive, yet flexible, workflow that allows the pathologist to view a whole-slide contextual scan and select regions for analysis using inForm. (a) Using whole slide multispectral imaging capabilities and Opal Polaris reagents, the entire digital slide is available for analysis using inForm without need to select fields for rescan. (b) The Vectra Polaris supports up to 9-color imaging and tissues stained with non-Opal reagents. Here, the pathologist can select any regions of interest for rescan using our LCTF technology for analysis using inForm.

TABLE 1. MANTA 2 SPECIFICATIONS

Mantra Instrument	
Imaging Modes	Brightfield and fluorescence, multispectral and color imaging
Microscope	<p>Customized research-grade microscope with:</p> <ul style="list-style-type: none"> · 8-position motorized epi-fluorescence filter turret · 7-position motorized objective nosepiece · Active management of intensity per-objective in Brightfield · Integrated ergonomic controls on microscope base
Camera Type	Multispectral 12-bit camera using cooled scientific-grade CCD
Camera Spectral Range	· 440 – 760, 780 nm for Brightfield imaging and Opal fluorophores
Objectives (Achromatic)	4X / 0.16 NA, 10X / 0.40 NA, 20X / 0.75 NA (40X / 0.95 NA optional)
Pixel Resolution	0.25 micron (optional 40X), 0.50 micron (20X), 1.0 micron (10X), 2.5 micron (4X)
Filter Cubes	<ul style="list-style-type: none"> · DAPI, FITC, Cy3, Texas Red, Cy5 · Optionally configured with Opal 780, Opal 480, or Quad-band for visualization
Fluorescence Illumination	6 Channel LED, >20,000 hour bulb life
Brightfield Illumination	High-output, color-balanced white LED
Physical Dimensions	
Width x Height x Depth	163 x 76 x 56 cm (Mantra workstation including: monitor, computer, keyboard/mouse, fluorescence illuminator)
Width x Height x Depth	145 x 76 x 56 cm (as above without computer)
Weight	24 kg (Mantra only)
Computer (Minimum Specifications)	
General	Quad-core, 16 GB RAM, i5 processors, mini-tower style
Hard Disk Drives (2)	500 GB for operating system and programs, 1 TB for data storage
Operating System	Windows 7/64
Interfaces	1 Gigabit Ethernet, USB
Monitor	29" flat-panel, 2560 x 1280 pixel resolution
Software	
Acquisition Software	Mantra Snap
Image Analysis Software	inForm Tissue Finder
Power Requirements	
Mantra Instrument - AC Input Power	100 - 230 VAC, 1.0A, 50/60 Hz
Fluorescence Illuminator - Input Power	100 - 240 VAC, 2.0A, 50/60 Hz

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