

Throughput, Sophistication, Robustness



WISCON® Hernes Throughput, Sophistication, Robustness

IDEA Bio-Medical presents a revolutionary technological platform for the drug discovery industry.

Hermes and other company products, driven by this technological platform, improve the output of drug discovery processes and bring down the exorbitant costs of biomedical and pharmaceutical R&D.

Major elements of the leading technology are WiScan® and WiSoft®:

WiScan®: IDEA Bio-Medical's High
Definition Cell Imaging technology for High
Content Screening processes (HCS), which
provides the unique combination of the
two contradicting primary features of
automated microscopy: Image Quality,
and Acquisition Speed.

WiSoft®: IDEA Bio-Medical's effective, proprietary analysis software, which provides a significant, sophisticated image processing algorithmic library, operated by a unique and simple software interface.

IDEA Bio-Medical was founded in 2007 through a partnership between YEDA (the Weizmann Institute's commercialization arm) and IDEA Machine Development, Design and Production Ltd. (an innovation hub).

Hermes is a cost-effective High Content / High Throughput Screening system that operates at extremely **high speeds** of image acquisition and generates very **high quality** images.

Hermes is **intuitively operated**. Its built-in applications are extremely **easy to use**, and are operated at the push-of-a-button.

The Hermes system is ideal for a large **variety of applications**, including Phenotypic Screening, Spheroids and 3D models, Rare-Event detection, Cytometry, Cell Count (cytotoxicity, proliferation), Protein Expression, Cell Morphology, Cell Cycle, Protein Translocation, Intracellular Vesicles Quantification, Golgi Intracellular Distribution, Mitochondria Characterization, Cytoskeleton Structure, Nuclear and Sub-Nuclear Structures Characterization, Bacteriology and Immunology.

Hermes is a **sophisticated and flexible** system, offering fluorescence colors, bright field option, Laser based photo bleaching and a large range of air objectives and oil objectives. The system can accommodate a variety of plates and sample formats.

Hermes is now offered with the unique capabilities of FRET and FRAP imaging processes.

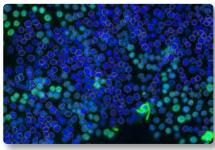
Hermes is a high-end, **attractively priced modular platform**, offering modular optional packages, which enable full customization for different user requirements.

Hermes' mechanisms are based on patents, creatively designed to meet heavy duty operation demands (24/7) with full process **robustness**.

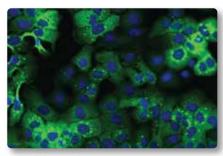
Hermes is a product of IDEA Bio-Medical, whose professional team is known for its creativity and for its responsiveness to customer for **support** and service.

Industry Trends are Challenged

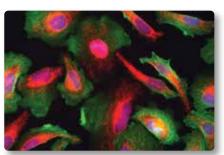




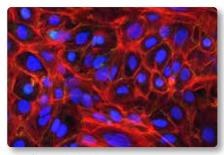
Cell Count (4x/0.16NA)



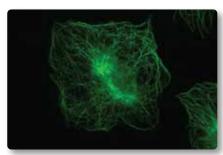
Intracellular Granules (10x/0.4NA)



Mitochondria, actin and nuclei (20x/0.75 NA)



Actin fibers and cell-cell junctions (40x/0.75NA)



Microtubules (60x/0.9NA)

Wiscon® Hermes Technology Advantages

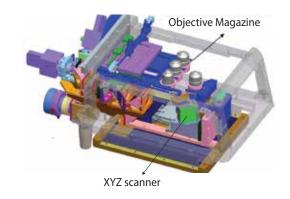
Patented XYZ Scanner

Patented XYZ scanner with 100nm resolution

- Consists of an optical path for illumination and image acquisition
- Holds 1 objective at a time the objective is the moving part while the plate remains stationary
- Equipped with linear motors and linear encoders for closed loop operation



- Special patented objective holder enables quick connect manually or automatically of Olympus objectives with no adjustment needed.
- Objective magazine holds 3 objectives
- Automatic loading of objectives to the scanner
- Offering 20 nm repeatability in positioning of the loaded objective





| Mag. | NA | Pixel Size (um) | Working Distance (um) |
|---------|------|-----------------|-----------------------|
| 2x | 0.08 | 3 | 6200 |
| 4x | 0.16 | 1.5 | 13000 |
| 10x | 0.4 | 0.6 | 3100 |
| 20x | 0.75 | 0.3 | 600 |
| 20x | 0.45 | 0.3 | 6600-7800 |
| 40x | 0.75 | 0.15 | 510 |
| 40x | 0.9 | 0.15 | 200 |
| 60x | 0.9 | 0.1 | 200 |
| 20x oil | 0.85 | 0.3 | 170 |
| 60x oil | 1.42 | 0.1 | 150 |

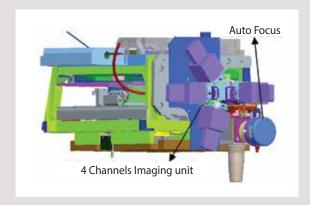
Objectives from different companies can be offered according to user's request.

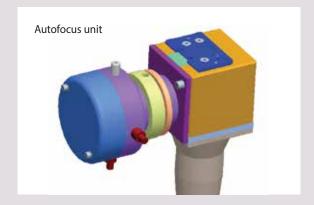
Multi Channel Imaging Module

- The imaging module consists of 1-4 imaging channels
- LED based fluorescence imaging with 2-7 optional wavelengths
- Brightfield using white LED illumination
- Laser based photo bleaching
- Image resolution ranges from 0.1 to 3 μm / pixel 60X-2X objective magnifications

Patented Autofocus

- Patented laser autofocus method with 100nm sample plane detection. Insures highly sharp images for full image segmentation reliability.
- Several algorithms are implemented for optimal performance in various magnifications.
- High throughput mapping for scanning U-shaped bottom plates used for spheroids and organoids imaging





Illumination Sources

- The Hermes is offered with up to 7 fluorescence colors, transmitted white LED light and laser diode used for photo bleaching in FRAP imaging process. Each of the fluorescence colors combination is offered with high/regular screening throughput configuration.
- Simultaneous acquisition mode for capturing rapid simultaneous events at maximum acquisition speed, is offered for specific color combinations.

| Fluorescence channel | Ex. | Em. | 7 color | HT 4 channels | HT 3 channels |
|-------------------------------|------------------------|--------|---------|---------------|---------------|
| DAPI | 390/18 | 440/40 | • | • | |
| CFP | 438/24 | 482/35 | • | • | • |
| FITC | 475/28 | 525/30 | • | • | |
| YFP | 513/17 | 542/27 | • | • | • |
| TRITC | 549/15 | 607/36 | • | • | |
| mCherry | 575/25 | 624/40 | • | • | • |
| CY5 | 648/20 | 694/44 | • | • | |
| Transmission White LED | Transmission White LED | | | | • |
| Laser Diode, 635nm, 5m | ıW | | • | • | • |

| Simultaneous acquisition combinations | Excitation (nm) | Emission (nm) |
|---------------------------------------|------------------|------------------|
| DAPI/HOECHST TRITC/Cy3 | 390/22 560/32 | 440/40 607/36 |
| DAPI/HOECHST CY5 | 390/22 648/20 | 440/40 694/44 |
| GFP/FITC CY5 | 485/25 648/20 | 525/30 694/44 |
| CFP mCherry | 485/25 575/35 | 525/30 624/40 |

Sample format

Maximum flexibility in plate formats. Any format with SBS standard may be used. Adaptors for slides, spotted array, dishes and chambers are available.



Hermes Configuration Options



Objectives (air):

- 2X/0.08
- 4X/0.16
- 10X/0.4
- 20X/0.45
- 20X/0.75
- 40X/0.75
- 40X/0.9
- 60X/0.9

Objectives (oil):

- · 20X/0.85
- 60X/1.42



Basic Imaging Module

• Filter wheel: 2-7 colors



Illumination sources

- DAPI (390/18: 440/40)
- CFP (438/24; 482/35)
- FITC (475/27; 525/30)
- YFP (513/17; 542/27)
- •TRITC (549/15; 607/36)
- mCherry (575/25; 624/40)
- CY5 (648/20; 694/44)
- Transmission white LED
- Laser diode 635nm



- High Throughput multi-channel imaging module: 3/4 colors select or 4-7/7 colors select
- Live cell environmental control
- Automation
- Object mapping for rare event detection
- WiSoft Minerva full analysis software





- Microplates (8-1536 wells)
- Slide holder
- Dish holder
- Chamber holder







1. Application selection

2. Scan Setup

3. Imaging Parameters Calibration

5. View Results

Ease of Use

- Simple and Intuitive user interface
- Fast and easy scanning setup
- Tablet-style touchscreen operation
- Joystick for sample navigation
- Extremely fast training



Multi Channel Imaging - High Throughput

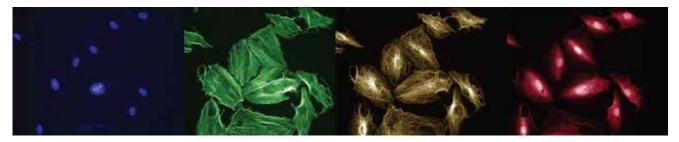
- Guarantees **m**aximum throughput
- Consists of monolithic passive unit with 2 to 4 selectable separate imaging channels
- Acquire images simultaneously (with no time gap or with a gap of exposure time only)



4 Channels Imaging module

High throughput acquisition rate is achieved in all range of magnification (2X-60X)
 by combination of the patented scanner, autofocus, multi-channel module for simultaneous imaging and software optimization.

| Plate Format | Colors | Fields per well | Exposure Time (msec) | Run Time (min: sec) |
|-----------------|--------|--------------------|-------------------------|------------------------|
| 96 | 4 | 1 | 50 | 01:39 |
| 384 | 4 | 1 | 50 | 05:25 |
| 1536 | 4 | 1 | 50 | 19:40 |

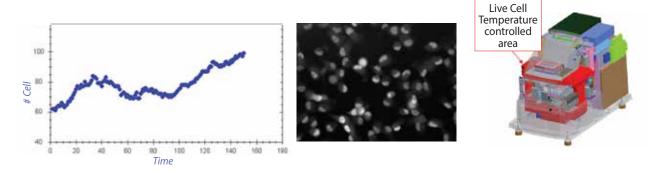


Multiplexing 4 cell features to evaluate cell status

Live Cell

Environmental stabilized conditions for live cells

- •Temperature control range from ambient+5°C to 40°C ± 0.5 °C CO2 controller as an external accessory.
- Allow long time lapse experiments with very high positioning repeatability (200nm).
- Microplate does not move along the scanning process.

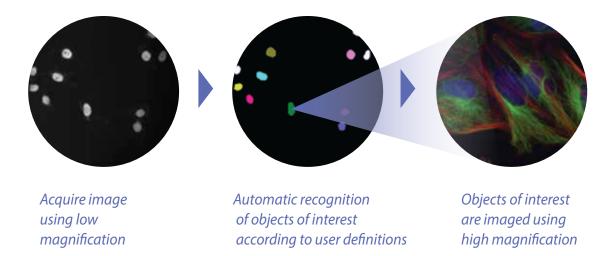


Proliferation assay - Analysis of cell number during treatment in live-fluorescently labeled H1299 cells (20x Magnification)

Object Mapping

Enhances throughput of high magnification screens by enabling recognition of islands of interest in low magnifications and imaging of those islands in higher magnification.

- Patented automatic objective exchanger with 20nm repeatability
- Run 2X-10X magnifications scan followed by 20X-60X High magnifications scan



Automation

Interfaces Hermes to Plate Stackers and Robotic Plate Handlers

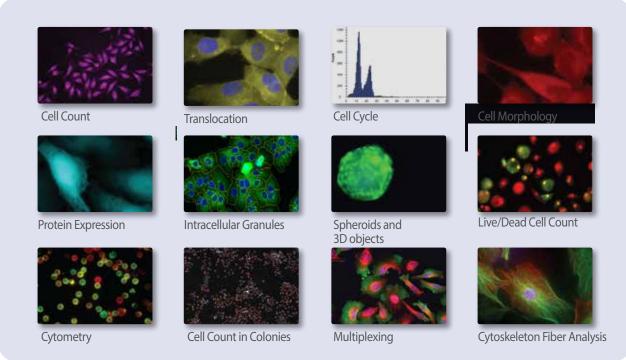
- Combination of SW and mechanical interface
- Remote accessibility
- External loader compatibility
- Automatic focus plane recognition
- Applied with numerous lab robots



Wiscon® Hermes Optional packages

WiSoft Athena- Application Software

- A software tool for application-derived analysis and visualization of image based experiments
- Incorporates embedded analysis algorithms, statistical evaluation tools and sub-population analysis
- The UI and UX are optimized for analyzing image-based cell biology experiments



WiSoft Minerva-Developers Software

- Environment for the development of analysis scripts
- Rich library of image analysis modules with unique algorithms optimized for fast analysis
- Sub-population analysis tools
- Variety of statistical evaluation modules
- Visualization tools
- Developer tools for incorporation of new analysis modules and for script debugging



WiScan Hermes system specifications

| Features | Content/Description |
|----------------------|---|
| 3D reader | EPI-fluorescent inverted optics mounted on XYZ (patented) linear scanner |
| Auto Focus | Patented ultra-fast laser based Auto Focus with 100nm resolution |
| XY motion | Accurate positioning with 200nm repeatability |
| Z motion | Accurate positioning with 100nm repeatability |
| Illumination sources | Fluorescence channels up to 7 optional LED sources. (DAPI, CFP, GFP, YFP, RFP, |
| | mCherry, CY5) Transmission: White LED source, laser diode 635nm |
| Optical Filters | Up to 7 emission filters and compatible dichroic filters. (automatically exchanged) |
| Objectives (Air) | Choice of air objectives ranging from 2X to 60X (see objectives table for details) |
| Objectives (Oil) | Optional 20X, 60X oil immersion objectives with automated oil feeding in closed loop |
| Camera | High sensitivity CCD camera 1.3MPixel |
| Image resolution | 0.1-3 um/pixel in 60X-2X objective magnification |
| Sample format | Supports full-area screening of 24-1536 well plates. Supports slides, microarrays |
| | and 35 mm dish formats. Supports U-shape bottom plates. |
| Computer | PC with Windows® operating system and touch screen. |
| Enclosure | Allows operation in fully lit areas |
| System Dimensions | Desktop standalone platform: 47 W x 72 D x 57 H (cm), 18.5 W x 28.5 D x 22.4 H (inches) |
| | With plate cover closed |
| Certification | CE, UL, FCC |
| | |

Acquisition Software specifications

| Features | Content/Description |
|--------------------------|--|
| Operation modes | Totally unattended screening Manual interactive microscope mode |
| Visualization | Interactive image and graphical data display |
| User Interface | User-friendly interface providing application-specific settings, |
| | full compatibility with the Athena software |
| Experiment Documentation | Full documentation of experimental parameters with the raw data |
| Image File Format | XML TIFF OME |
| Connectivity | Data transfer and remote monitoring via a network connection |

User's Scientific Publications

Chemistry Communications, 2014, 5, 1863-1870

GRP78 / BiP / HSPA5 / Dna K is a universal therapeutic target for human disease Booth L., Roberts J.L., Cash D.R., Tavallai S., Jean S., Fidanza A., Cruz-Luna T., Siembiba P., Cycon K.A., Cornelissen C.N., Dent P.; Journal of Cellular Physiology, 2015, 230(7): 1661-76 Variomics screen identifies the reentrant loop of the calciumactivated chloride channel ANO1 that facilitates channel activation Bill A., Oana Popa M., van Diepen M.T., Gutierrez A., Lilley S., Velkova M., Acheson K., Choudhury H., Renaud N.A., Auld D.S., Gosling M., Groot-Kormelink P.J., Alex Gaither L.G.; Journal of Biological Chemistry, 2015, 290: 889-903 3,5-Diamino-1,3,4-triazoles as a novel scaffold for potent, reversible LSD1 (KDM1A) inhibitors. Kutz C.J., Holshouser S.L., Marrow E.A., Woster P.M.; Medicinal

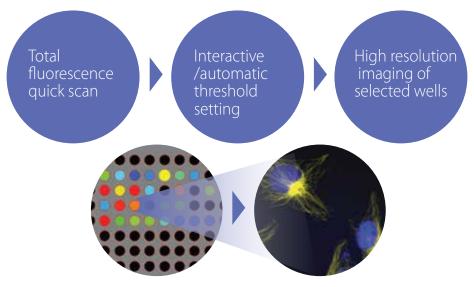
The Cofilin Phosphatase Slingshot Homolog 1 (SSH1) Links NOD1 Signaling to Actin Remodeling.
Bielig H., Lautz K., Braun P.R., Menning M., Machuy N., Brugmann C., Barisic S., Eisler S., Andree M., Zurek B., Kashkar H., Sansonetti PJ, Hausser A., Meyer TF, Kufer TA; PLOS Pathogens, 2014, 10, 9.
Regulation of OSU-03012 Toxicity by ER Stress Proteins and ER Stress-Inducing Drugs.
Booth L., Roberts J.L., Cruickshanks N., Grant S., Poklepovic A., Dent P.; Mol. Cancer. Ther, 2014, 1–15, AACR HIV-1 evades innate immune recognition through specific cofactor recruitment.
Rasaiyaah J., Tan C.P., Fletcher A.J., Price A.J., Blondeau C., Hilditch

L., Jacques D.A., Selwood D.L., James L.C., Noursadeghi M., Towers

G.J.; Nature, 2013 Nov 21;503(7476):402-5

Multiscale Imaging

- Multimode scan: quick total fluorescence scan followed by interactive definition of selected wells with high resolution objective.
- Speed of initial scan 1-5 min (96-1536 well plates)
- From total well signal to selected wells detailed imaging



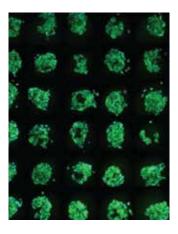
Slide Imaging

- Single ROI or spotted array format
- Interactive scan region selection.
- Special slide holder. Option for custom design.

| Adaptor | Cat# |
|-----------|----------|
| Slide | 10064807 |
| Chamber 🗔 | 10064818 |
| Dish | 10064866 |



Mouse brain. Montage using 10X magnification



Biochip with labeled cells plated on adhesion spots

Time Lapse

- Multi -time point scanning
- Option to select a point list for re-visiting
- Maximum rate of acquisition in a single spot 14 Hz
- Flexible definition of cycles and intervals

Z stack

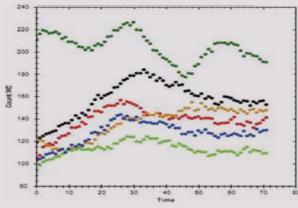
- Multi Z plane scanning
- Interactive definition of the distance between planes and the number of planes
- Interactive definition of upper and lower scan plane
- Option for combination with time lapse, rare event and all biological applications

Fluorescence Recovery After Photobleaching (FRAP)

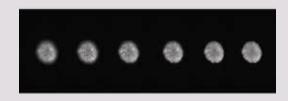
- Adaptation of FRAP for high content screening
- Bleaching is conducted by diode laser beam
- Diffusion information and fraction of diffusing component calculated from the data using dedicated Athena application
- Optional HTS mode where only 3 time points are acquired: pre-bleaching, post bleaching and after recovery
- Sequential or per field acquisition

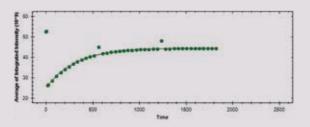
Fluorescence Resonance Energy Transfer (FRET)

- High resolution high throughput FRET imaging.
- FRET signal indicates close proximity between the fluorophores.
- Measures the emission of an acceptor molecule after energy transfer from a donor fluorophore
- Excitation using LED
- Flexible donor and acceptor definition



Count and Fluorescence as a Function of Time







wiscon[®] Hermes







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