Phenotype MicroArrays

for Mammalian Cells.

Using Biolog's Phenotype MicroArray™ Technology, any type of cell can be characterized for metabolically related phenotypes in over 1,000 assays in a simple, rapid, and cost-effective manner. By measuring a cell's metabolic activity, including responses to a genetic alteration or chemical stimuli, this integrated system of cellular assays, instrumentation, and bioinformatic software reveals unique and insightful information on metabolic pathway activities, and cellular sensitivity to nutrients, hormones, cytokines, anti-cancer agents, and ions. By measuring energy output of cells, the technology also provides new assays for understanding mitochondrial function and toxicity.

Phenotype MicroArrays enable insight and discovery to expedite scientific publications.

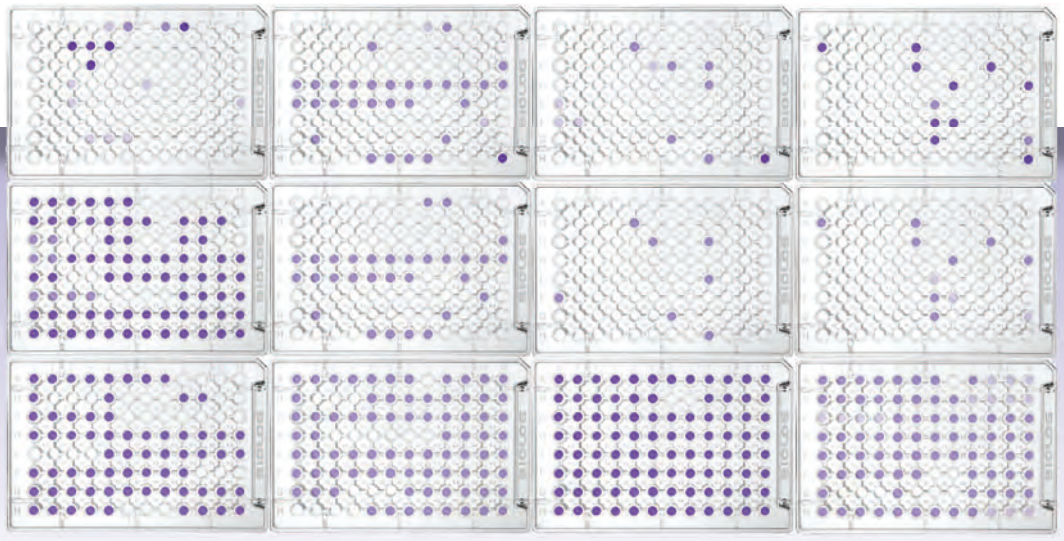
This is accomplished using 96 well microplates, pre-loaded with hundreds of KEGG pathway-matched metabolic substrates, and metabolic effectors.

Phenotype MicroArrays are a proven method of cellular screening that is beneficial in a wide range of research applications:

- Genotype/phenotype studies
- Cell line characterization and QC
- Cellular metabolism, metabolic disorders, nutrition
- Cell energetics growth and death
- Hormone effects on cells
- Metabolic reprogramming in cancer, Warburg effect, anti-cancer drug sensitivity
- Mitochondrial toxicology in chemical/drug screens
- Stem cells and differentiation
- Cell line and bioprocess development

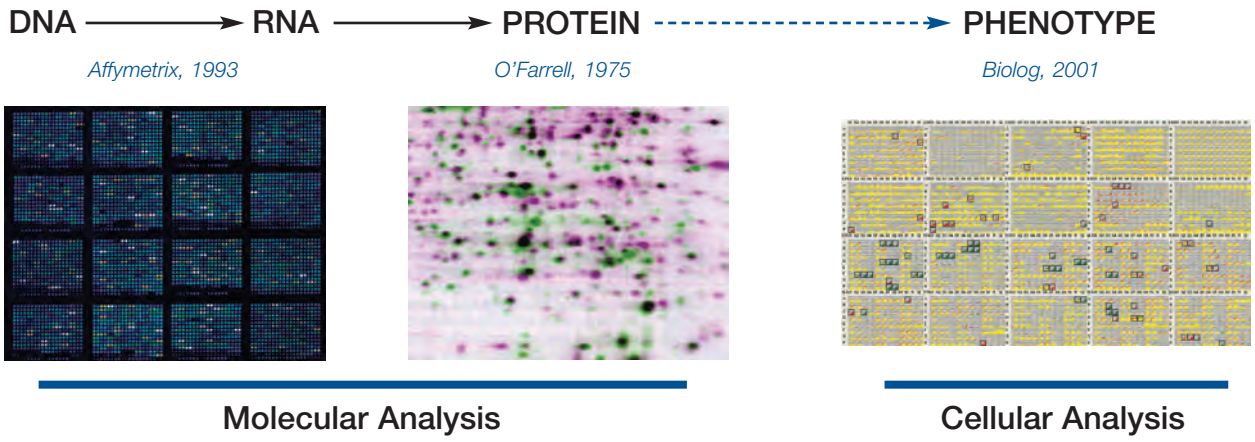
The Biolog OmniLog® simultaneously incubates and monitors 50 microplates with thousands of phenotypic assays to measure physiological responses in diverse mammalian cells.

BIOLOG



A BREAKTHROUGH TECHNOLOGY

Phenotype MicroArrays represent the fourth major technology, *"Phenomics"*, alongside Transcriptomics, Proteomics, and Metabolomics that are needed in the genomic era. Just as the molecular assay technologies have made it possible to analyze gene transcript or protein or metabolite levels in the cell, Phenotype MicroArrays make it possible to quantitatively measure thousands of cellular phenotypes by analyzing live cells in real time. Molecular assay technologies require cell disruption so each analysis represents a sampling of the cell at a single time point. From this, scientists can detect genes or proteins that are coregulated and whose patterns of change correlate with something important such as a disease state. However there is no assurance that these changes are really significant to the cell. Phenotype MicroArrays are a complementary technology providing the needed information at the cellular level ... and much more. Phenotype MicroArrays, provide comprehensive cellular profiles that can be used to identify gene function, determine changes in cell metabolism, elucidate drug effects, and even improve cell growth and productivity in bioprocess optimization. After a genetic change or exposure to a drug or a nutrient, the researcher can directly evaluate the cellular response to that change.

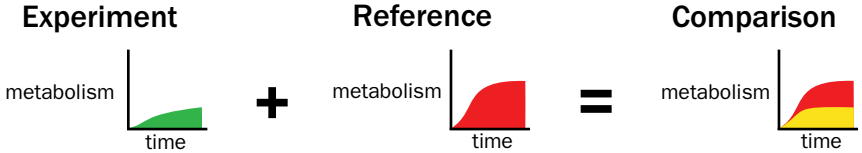


HOW PHENOTYPE MICROARRAY TECHNOLOGY WORKS

Phenotype MicroArrays are preconfigured sets of phenotypic tests deployed on MicroPlate panels. Each well of the array is designed to test a different phenotype after inoculation with a standardized cell suspension, allowing simultaneous testing of thousands of phenotypes in a single experiment. Phenotype MicroArrays use Biolog's patented redox technology, to measure cell energy (NADH) production as a universal reporter. If the phenotype is strongly "positive" in a well, the cells actively generate energy and reduce a tetrazolium dye, forming a strong color. If it is weakly positive or negative, energy production is slowed or stopped, and less color or no color is formed. The redox assay provides for both amplification and precise quantitation of phenotypes.

Incubation and recording of phenotypic data is performed automatically by the OmniLog® instrument, which captures a digital image of the Phenotype MicroArray several times each hour and stores the quantitative color change values into computer files. The computer files are then displayed in the form of kinetic graphs. In one OmniLog run, up to 4800 assays can be performed.

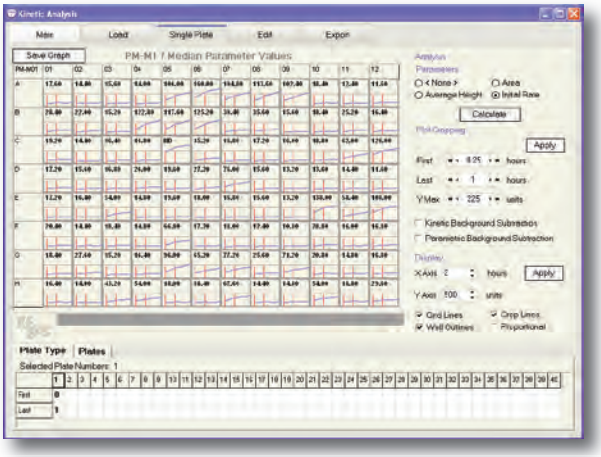
To compare the phenotypes of two cell lines, one is recorded as a red tracing and one as a green tracing. These graphs can then be overlaid by the bioinformatic software to detect differences. Areas of overlap (i.e. no phenotypic change) are colored yellow, whereas differences in phenotypes are highlighted as patches of red or green.

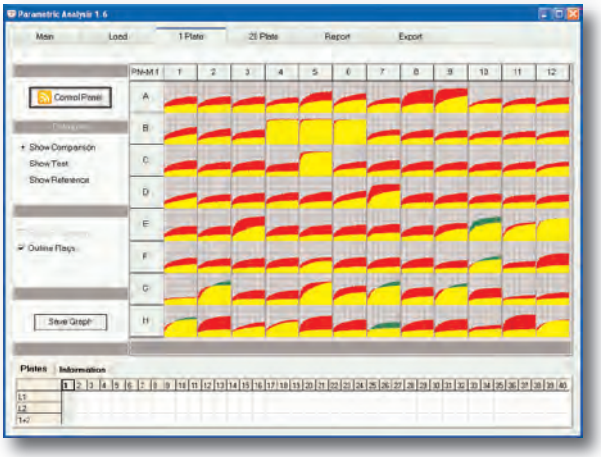


KINETIC DATA CAPTURE AND ANALYSIS

OmniLog PM-M software contains a suite of algorithms that work in conjunction with the OmniLog PM-M system and Phenotype MicroArray panels to automate incubation of up to 50 microplates at a user-specified temperature with continuous collection of colorimetric assay data over time. PM-M data analysis programs allow for display of kinetic data, manage and analyze the data, export it in a variety of raw and processed forms, and generate reports.

Many Parameters are calculated from Kinetic Plots by PM Software





OmniLog Software Functions

- Drives the operation of the OmniLog PM-M System
- Guides loading and reading of PM-M panels
- Creates a kinetic data file for each PM-M panel

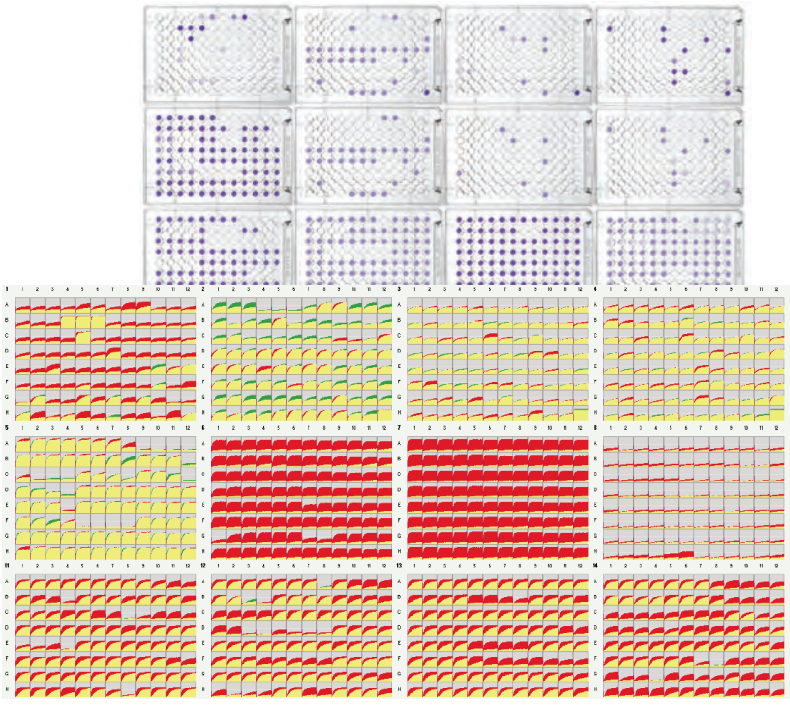
File Management/Kinetic/Parametric Analysis

- Assembles plate or PM-M panel data files into data lists
- Displays kinetic plots of the data
- Allows export of kinetic plots as bmp or jpeg files
- Extracts data lists from the File Management /Kinetic Analysis module
- Calculates parameters from kinetic data
- Allows comparison of two data lists
- Highlights wells and generates a report on phenotypes that differ significantly in any selected kinetic analysis parameter
- Allows identification of substrates in all PM-M panels
- Links metabolic substrates in PM-M panels to the KEGG database
- Exports the original OmniLog kinetic data
- Exports data parameters for statistical and bioinformatic analysis

OmniLog-PM's PMM Assay Portfolio

(Assay plates available individually. Specific details on substrates and effectors can be found on Biolog's website)

- **Carbon Energy & Nitrogen Substrates:** 367 metabolic substrates. Substrates include carbohydrates/starches, alcohols, fatty acids, ketones, carboxylic acids, amino acids and dipeptides on 4x96 well microplates
- **Hormones:** 45 different hormones each at six different concentrations on 3x96 well microplates
- **Trace Elements:** 22 different ions/cofactors each at four different concentrations on 1x96 well microplate
- **Anti-Cancer Chemosensitivity:** 92 anti-cancer agents each at four different concentrations on 4x96 well microplates
- **Mitochondrial Toxicity:** 8 carbon-energy substrates (associated with diverse pathways, e.g. hexose, pentose, etc.) to distinguish different aspects of mitochondrial activity/dysregulation in the context of chemical/drug screens on 1x96 well microplate



Phenotype MicroArray Applications

Phenotype MicroArray Technology is now available for applications with nearly all important cell lines.

General Areas Emphasizing Metabolism:

- *Obesity*
- *Diabetes*
- *Metabolic Disorders*
- *Nutrition*
- *Aging*
- *Mitochondrial Diseases*
- *Cancer (Warburg Effect)*
- *Chemosensitivity*
- *Mitochondrial Toxicity*
- *Cellular Toxicity*
- *Stem Cell Metabolism*
- *Bioprocess Optimization*
- *Cell Line QC*
- *Cell Energetics*

OmniLog PM-M System Specifications

The PM-M system includes: instrument, computer, LCD flat panel monitor, software for data collection and analysis, 8 & 12 channel electronic pipettors, user guide, training and one year warranty. Consumables and other accessories are purchased separately.

Size: 21 in x 32 in x 23 in (53 cm x 81 cm x 58 cm)

Power: 100 to 240 volts, 50 to 60 Hz

Operating Temp Range: 18˚ to 28˚C

Operating Humidity Range: 20% to 80% non-condensing

Incubation Temperature Range: 20˚ to 45˚C

Temp Consistency: ±2˚C in the tray chamber

Incubation Humidity Range: Ambient

Test Capacity: 50 microplates

Data Capture: CCD images of each microplate at regular intervals

Temperature Control: Input of set temperature by external computer

Temperature Indication: Output to external computer and LED numeric display

BIOLOG

BIOLOG, Inc.
21124 Cabot Blvd, Hayward, CA 94545 USA
(510) 785-2564 • www.biolog.com

Part #00A 046 Rev A 02/2013