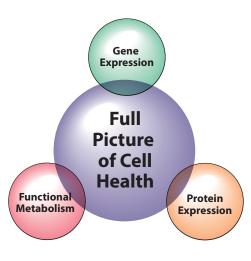
FUNCTIONAL METABOLIC ASSAYS

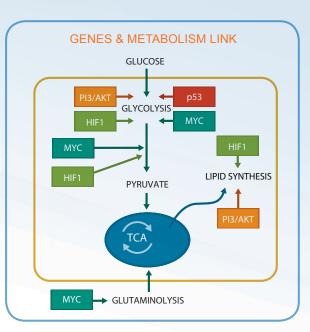
THE GENOTYPE-PHENOTYPE LINK

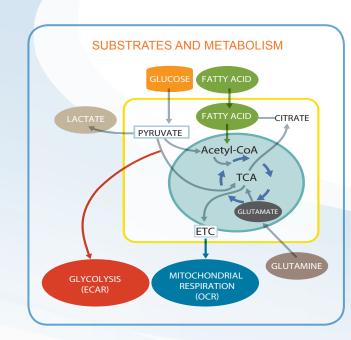
The traditional paradigm encompassing the flow of information from gene to protein to function can be found in nearly every biology and biochemistry textbook. At the time, this discovery was thought to explain all of biology, health, and disease. However, only focusing on the expression of a single gene or protein neglects the multi-faceted consequences of that expression on metabolism, as well as overall cell and tissue health.

Mitochondria are at the crux of cellular energy generation, intracellular signaling, and cell death and survival regulation. Compromised mitochondria can strain the expansive and intricate cellular metabolic network. There is increasing appreciation for the role of mitochondria in disease pathology, etiology, and cell health.

Integrating processes that demonstrate the link amongst genes, proteins, and metabolism allows researchers to analytically answer their scientific questions. XF Technology provides researchers the necessary tools to measure the functional, metabolic impact of gene and protein expression, faster and easier using live cells.



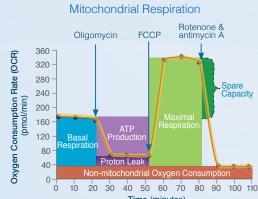




GOLD STANDARD METABOLIC ASSAYS

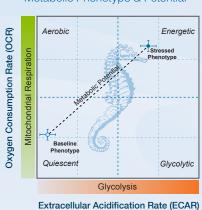
MEASURING THE KEY PARAMETERS OF CELL METABOLISM

XF Cell Mito Stress Test Profile

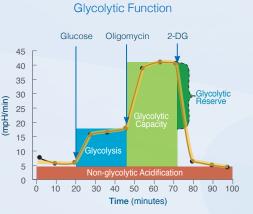




XF Cell Energy Phenotype Test

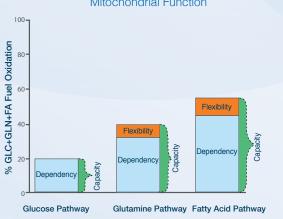


XF Glycolysis Stress Test Profile Glycolytic Function



XF Mito Fuel Flex Test Profile





GENE-PROTEIN-METABOLISM LINKS

Cell Metabolism Assays Research



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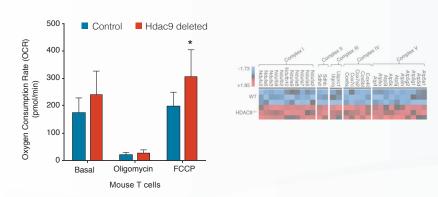


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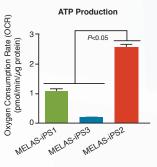
STANDARD PARAMETERS OF FUNCTIONAL METABOLISM

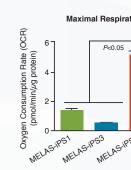
GENOMICS

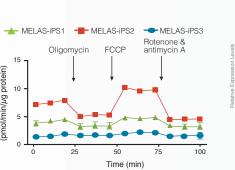
Cells use gene expression to synthesize proteins and other products that are essential for various cellular functions. Gene expression levels, while associated with metabolism, cannot solely predict the functional impact on metabolism. This creates a gap in understanding the complex physiological relation between genes and metabolism. Researchers are using XF Technology to link functional metabolism to gene expression for a complete picture. The XF Cell Mito Stress Test measures the key parameters of mitochondrial respiration: basal respiration, ATP-linked respiration, maximal respiration, and spare respiratory capacity. The XF Glycolysis Stress Test measures the key parameters of glycolytic activity: glycolysis, glycolytic capacity, glycolytic reserve.



XF Assay reveals a link between histone deacetylase 9 (Hdac9) deletion and mitochondrial respiration correlating to a genetic and functional increase in T regulatory cells. (Beier UH et al., 2015. FASEB J.)







Human neuronal progenitor cells

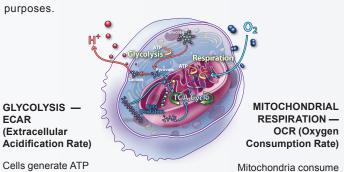
XF Cell Mito Stress Test predicts differentiation status in neuronal progenitor cells (NPCs) derived from patients with mutations causing mitochondrial encepharopathy and stroke-like episodes (MELAS) which correlates to gene expression

(Ma H et al., 2015. Nature.)

THE WORLD'S MOST ADVANCED METABOLIC ANALYZERS

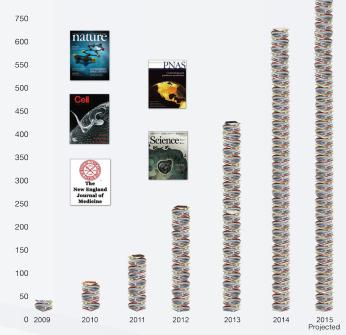
PROVEN TECHNOLOGY FOR CUTTING EDGE RESEARCH

There are over 2,000 references utilizing XF Technology published in leading journals such as Nature and Cell. Scientists are embracing XF Technology to identify metabolic phenotypes and reprogramming to target metabolic pathways for therapeutic



oxygen when oxidizing fatty and protons. XF Analyzers measure to generate ATP. XF glycolysis by measuring the extracel-Analyzers measure mitochondrial lular acidification rate (ECAR) of respiration by measuring the oxygen

consumption rate (OCR) of cells.



PROTEOMICS

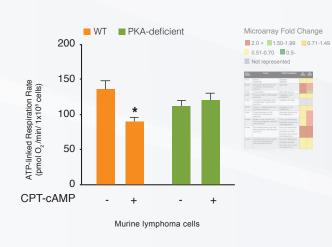
ECAR

(Extracellular

via glycolysis independent

of oxygen, producing lactic acid

Advances in proteomic technology enables genome-wide data analysis, pinpointing specific proteins and expression levels. Proteomic data directly links to metabolism without requiring the regulatory mechanisms associated with mRNA expression and final protein expression. However, conclusions utilizing only these types of experiments are limited. XF Technology not only confirms proteomic data but also allows for further investigation of protein function.



XF Cell Mito Stress Test reveals that protein kinase A (PKA)dependent changes in protein and gene expression correlate with changes in ATP-linked respiration. Wilderman A et al., 2015. J Biol Chem.)

→ GM-BMM -A-M-BMM Murine bone-derived macrophages XF Glycolysis Stress Test reveals the increased glycolytic capacity

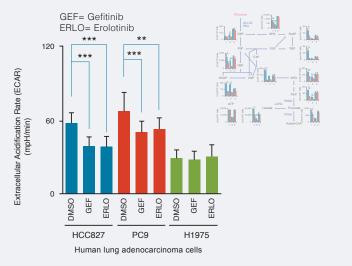
of granulocyte-stimulated macrophages (M-BMM), confirming the inherently higher glycolytic protein expression.

(Na YR et al., 2015. Mol Cell Proteomics.)

MEASURING THE KEY PARAMETERS OF FUNCTIONAL CELL METABOLISM

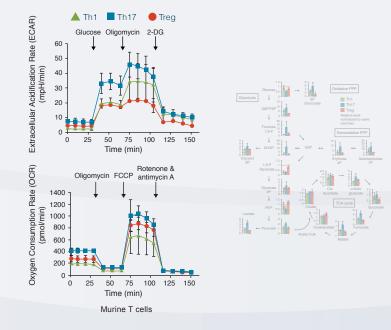
METABOLOMICS

Techniques, such as mass spectrometry (MS) and nuclear magnetic resonance (NMR), enable the analysis of hundreds of metabolites in a given sample. However, the data from these techniques alone are not sufficient to assess functionality within a biological context. XF Technology provides real-time analysis of cellular response to stress or nutrients, and can direct metabolomics research, adding efficiency and direction to any area of research.



XF Glycolysis Stress Test predicts sensitivity to first-line EGFR inhibitors used in lung adenocarcinoma cells, and correlates to reduced metabolite levels.

(Makinoshima H et al., 2014, J Biol Chem.)



XF Glycolysis Stress Test and XF Cell Mito Stress Test reveal increased levels of mitochondrial respiration and glycolytic activity in TH17 (T cells) which correlate to changes in metabolite levels.

(Gerriets VA et al., 2015. J Clin Invest.)

WHAT OUR CUSTOMERS ARE SAYING

"We were really surprised by the impact of measuring metabolism in our model system. This opens up new research avenues for us." Researcher at Rosalind Franklin

"With very little learning curve, XF Technology provides highquality data. We generated publishable results within the first month."

- Researcher at Case Western Reserve University

Medical School

"When we decided to more closely investigate branched chain amino acid metabolism, we chose to incorporate our XF Technology, knowing that it is a powerful tool for assessing mitochondrial function and metabolism."

Researcher at University of



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