THE CANCER-METABOLISM LINK

Cell Metabolism Assays for Cancer Research

Seahorse *Bioscience*

A part of **Agilent Technologies**

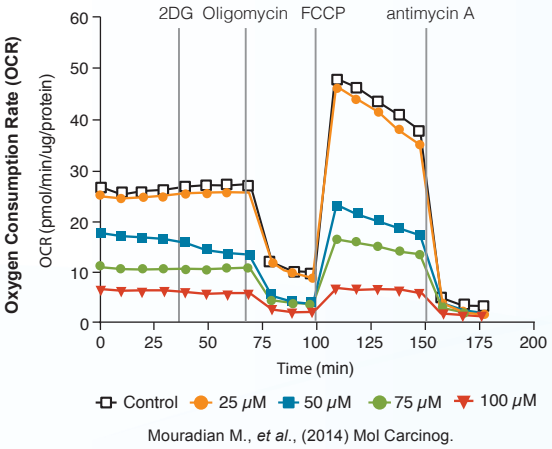
MEASURING THE KEY PARAMETERS OF CANCER METABOLISM

METABOLIC PHENOTYPES OF CANCER CELLS

Cancer cells exhibit a phenotype that reflects their metabolic needs. Researchers are using Seahorse XF technology and XF stress tests to explore these metabolic changes, and the effect of metabolic therapies to increase their understanding of cancer. The Seahorse XF Cell Mito Stress Test measures the key parameters of respiration: basal respiration, proton leak, ATP-linked respiration, maximal respiration, and spare respiratory capacity. The Seahorse XF Glycolysis Stress Test measures the key parameters of glycolytic function: glycolysis, glycolytic capacity, and glycolytic reserve.

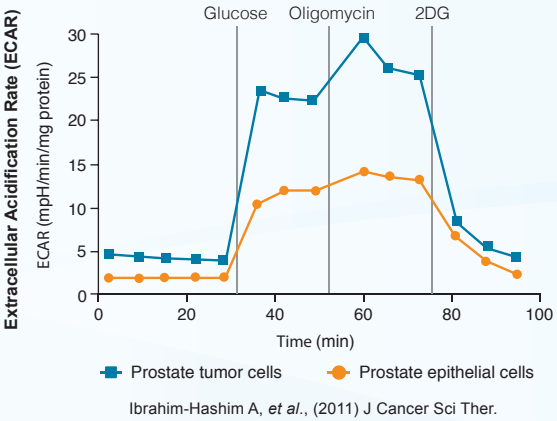
METABOLIC PROFILES

Cancer cells have a metabolic profile which reflects their altered bioenergetic requirements to support proliferation.



Mouradian M., *et al.*, (2014) Mol Carcinog.

Seahorse XF Cell Mito Stress Test reveals the dose-dependent susceptibility of breast cancer cells to polyunsaturated fatty acids as shown by a depression in all parameters of mitochondrial respiration.

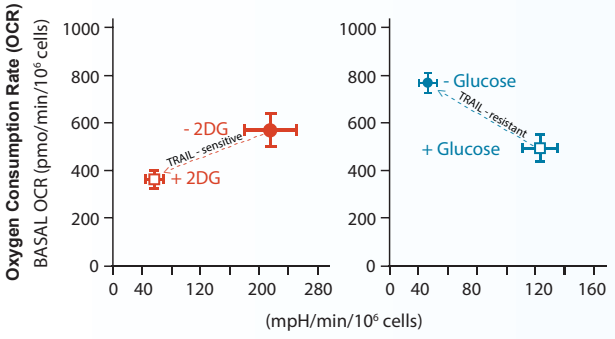


Ibrahim-Hashim A, *et al.*, (2011) J Cancer Sci Ther.

Seahorse XF Glycolysis Stress Test identifies prostate tumor cell susceptibility to buffer therapy illustrated by an increased glycolytic capacity over normal prostate epithelial cells.

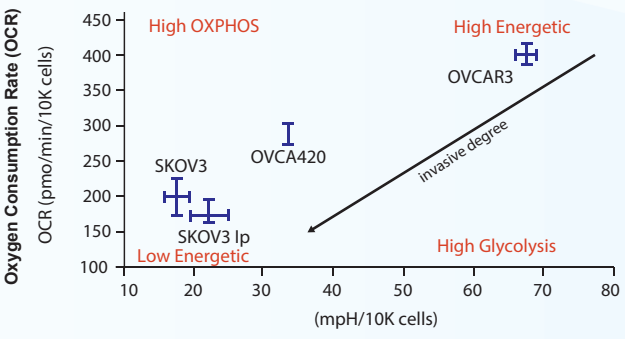
METABOLIC SWITCHING

Cancer cells are known to switch to a metabolic phenotype that drives proliferation, such as shifting towards glycolysis (known as the Warburg effect), as illustrated by these Seahorse XF phenograms.



Robinson GL., *et al.*, (2012) Oncogene

Seahorse XF Metabolic Switch Assay illustrates a Reverse Warburg phenotype in mantle cell lymphomas sensitive to TRAIL induced by 2DG inhibition, unlike the prototypic Warburg switch to aerobic glycolysis in the presence of glucose (TRAIL-resistant).



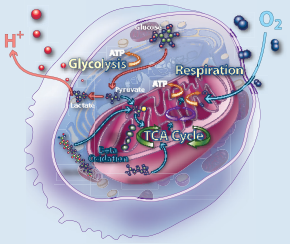
Yang L., *et al.*, (2014) Mol Syst Biol.

Seahorse XF Metabolic Switch Assay identifies highly invasive ovarian cancer cells which have decreased energetics.

THE WORLD'S MOST ADVANCED METABOLIC ANALYZERS

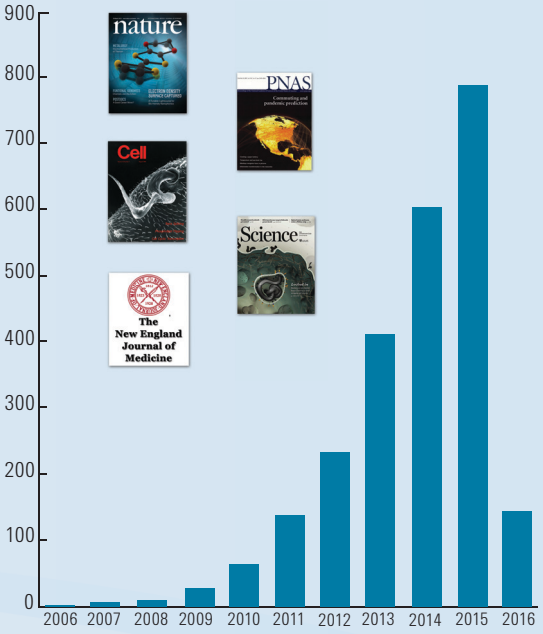
XF DATA IN PUBLICATIONS

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



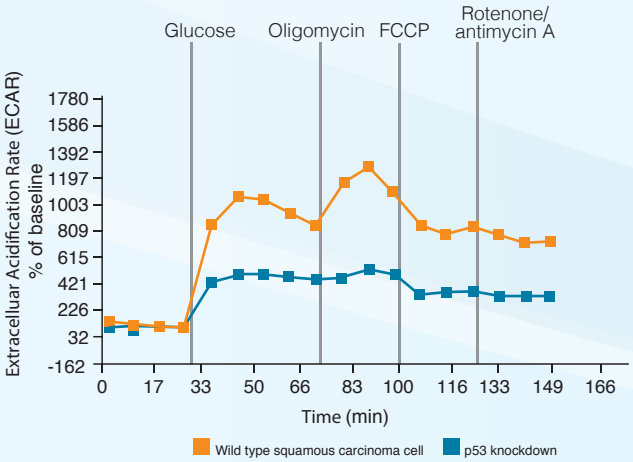
Glycolysis
ECAR (Extracellular Acidification Rate)

Mitochondrial Respiration
OCR (Oxygen Consumption Rate)



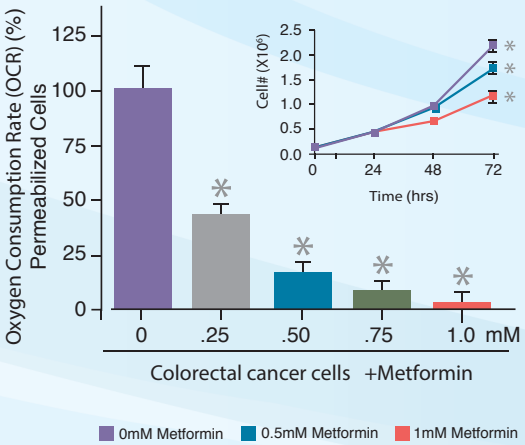
PATHWAYS AND MECHANISM OF ACTION IN CANCER CELLS

Cancer therapies have exploited rapid proliferation as a treatment option. These treatment options can result in unwanted and unacceptable side effects. Using Seahorse XF technology to focus on understanding cell metabolism, more selective therapeutic agents can be studied and explored, not only for the effect on cancer cells, but for their systemic effects as well.



Zhou G., *et al.*, (2014) Mol Cell.

Seahorse XF assay reveals p53 pathway is critical for reversing Warburg metabolism illustrated by reduced glycolytic activity in p53 knockdown squamous carcinoma cells.



Wheaton W., *et al.*, (2014) eLife

Seahorse XF assay reveals an unexpected dose-dependent metformin inhibition of complex I correlating to proliferation in colorectal cancer cells.

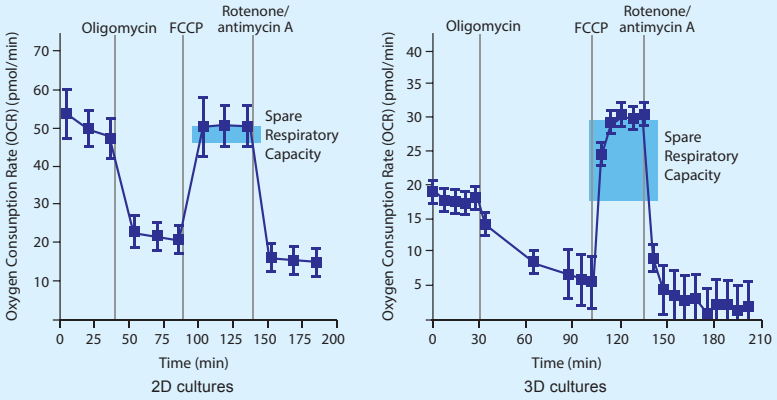
XF ASSAYS FOR THE METABOLIC HALLMARKS OF CANCER

TUMOR MICROENVIRONMENT

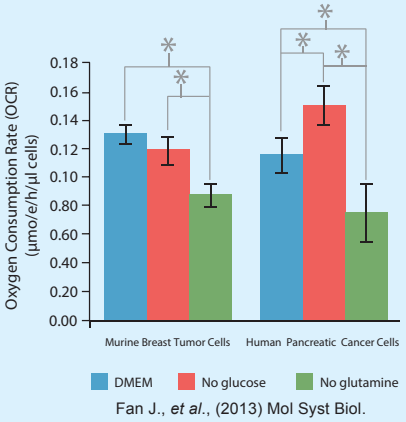
To mimic a tumors' *in vivo* environment, researchers employ methods such as culturing cells under hypoxia or modeling tumors as multicellular spheroids. Seahorse XF technology is capable of adapting to a variety of culturing conditions to provide precise, *in vivo*-like, physiologically relevant metabolic data.

HYPOXIA AND SPHEROIDS

Tumors are heterogeneous and exist in a complex, 3D environment defined by nutrient and chemical gradients (O_2, pH, etc.).



Seahorse XF technology enables precise metabolic measurements in 3D cultures as illustrated by an increase in spare respiratory capacity in 3D cultures of colorectal cancer cells.

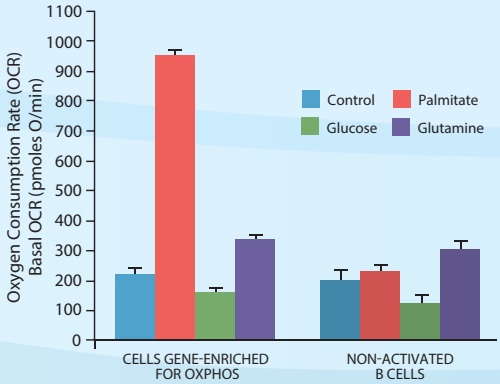


Fan J., *et al.*, (2013) Mol Syst Biol.

Seahorse XF technology reveals glutamine oxidation requirement for hypoxia survival in both murine breast cancer and human pancreatic cells.

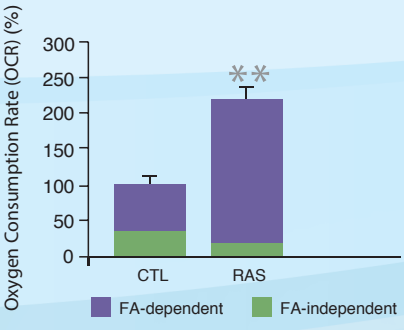
SUBSTRATE PREFERENCE

Cancer cells alter their substrate preference to maintain their rapid proliferation. Seahorse XF technology provides the necessary tools that facilitate the exploration of substrate preferences,enabling a greater understanding of cancer cell progression.



Caro P., *et al.*, (2012) Cancer Cell.

Seahorse XF assay identifies substrate preference of lymphoma subsets.



Quijano C, *et al.*, (2012) Cell Cycle

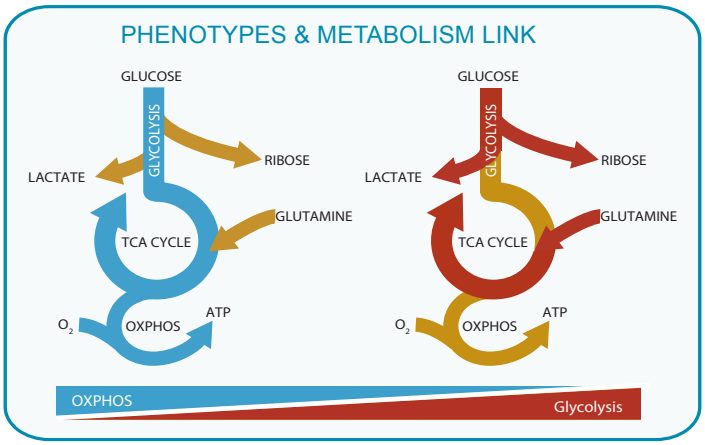
Seahorse XF assay reveals the critical role of fatty acid oxidation in Ras-mediated senescence of fibroblasts.

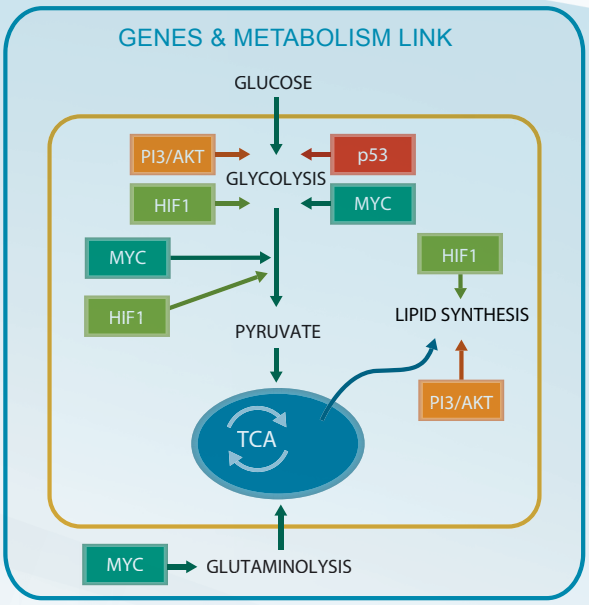
THE CANCER-METABOLISM LINK

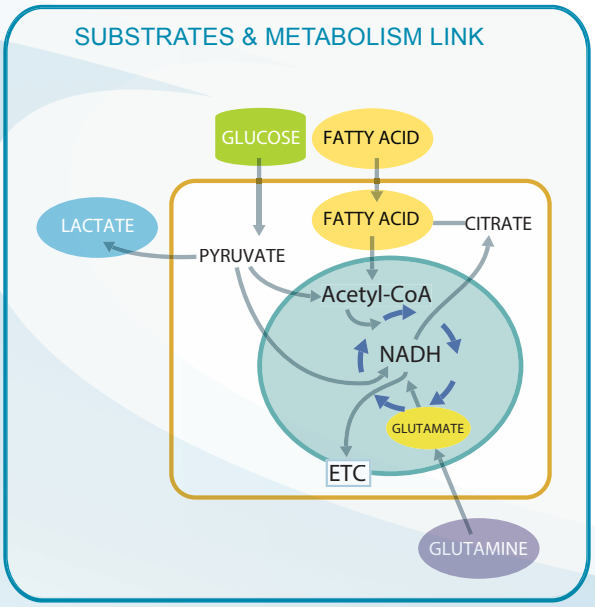
XF assays measure the hallmarks of cancer: oncogene reprogramming of metabolism, substrate preference of tumor cells, and metabolic phenotypes.

Proliferation, associated with carcinogenesis, involves oncogenes, proto-oncogenes, and mutated tumor-suppressor genes. Rapid proliferation correlates to the cells' metabolic phenotype. To maintain rapid growth cancer cells will reprogram their metabolic phenotype,switching between glycolytic and aerobic phenotypes.

Cancer cells change their substrate preference as they alter their metabolic phenotypes. For example, cancer cells may increase glutamine metabolism, alter lipid metabolism, or shift the balance between anabolic and catabolic processes. There is increasing evidence of the interactions amongst genes, substrates, and phenotypes. Seahorse XF technology and assays are bringing unique value to investigate the mechanisms behind the hallmarks of cancer and altered cell metabolism.



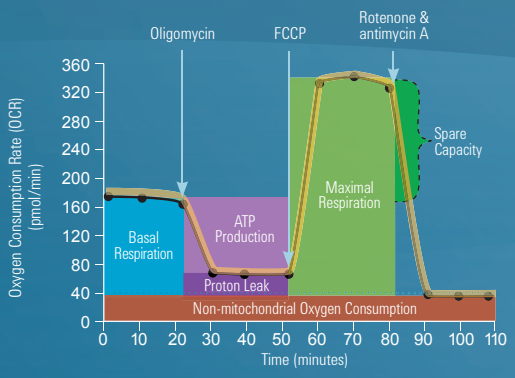




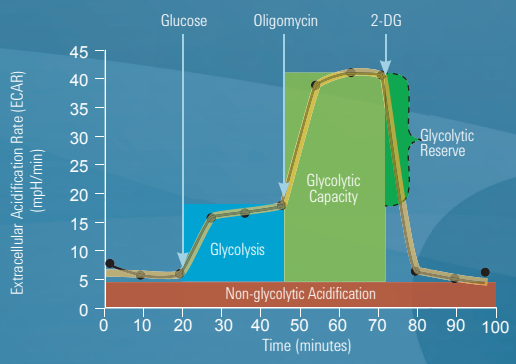
XF METABOLIC ASSAYS

MEASURING THE KEY PARAMETERS OF CELL METABOLISM

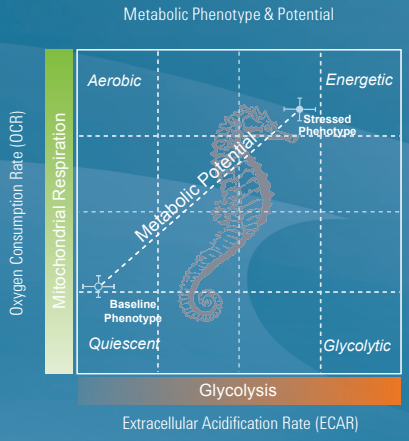
Seahorse XF Cell Mito Stress Test Profile



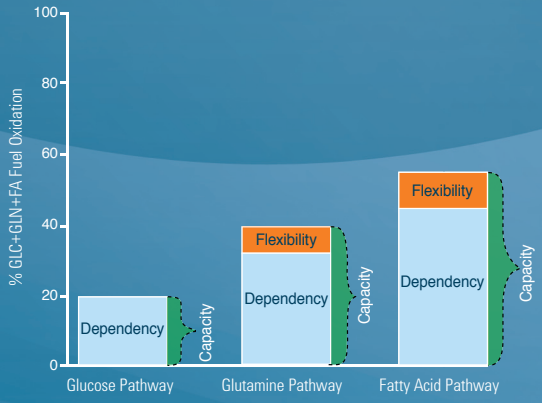
Seahorse XF Glycolysis Stress Test Profile



Seahorse XF Cell Energy Phenotype Test



Seahorse XF Mito Fuel Flex Test Profile



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