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 XF Technology and XF Stress Tests to explore these metabolic changes, and the effect of metabolic therapies to increase their understanding of cancer. The 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 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.

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 XF Phenograms.

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**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.

**XF Glycolysis Stress Test**

Identifies prostate tumor cell susceptibility to buffer therapy illustrated by an increased glycolytic capacity over normal prostate epithelial cells.

**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).

**XF Metabolic Switch Assay**

Identifies highly invasive ovarian cancer cells which have decreased energetics.
Cancer therapies have exploited rapid proliferation as a treatment option. These treatment options can result in unwanted and unacceptable side effects. Using 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.

**PATHWAYS AND MECHANISM OF ACTION IN CANCER CELLS**

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

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

To mimic a tumors' in vivo environment, researchers employ methods such as culturing cells under hypoxia or modeling tumors as multicellular spheroids. 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 (O₂, pH, etc.).

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.

SUBSTRATE PREFERENCE

Cancer cells alter their substrate preference to maintain their rapid proliferation. XF Technology provides the necessary tools that facilitates the exploration of substrate preferences, enabling a greater understanding of cancer cell progression.
THE CANCER-METABOLISM LINK

XF Gold Standard 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. XF Technology and the Gold Standard assays bring unique value to investigate the mechanisms behind the hallmarks of cancer and altered cell metabolism.
GOLD STANDARD METABOLIC ASSAYS
MEASURING THE KEY PARAMETERS OF CELL METABOLISM

**XF Cell Mito Stress Test Profile**
Mitochondrial Respiration

**XF Glycolysis Stress Test Profile**
Glycolytic Function

**XF Cell Energy Phenotype Test**
Metabolic Phenotype & Potential

**XF Mito Fuel Flex Test Profile**
Mitochondrial Function

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