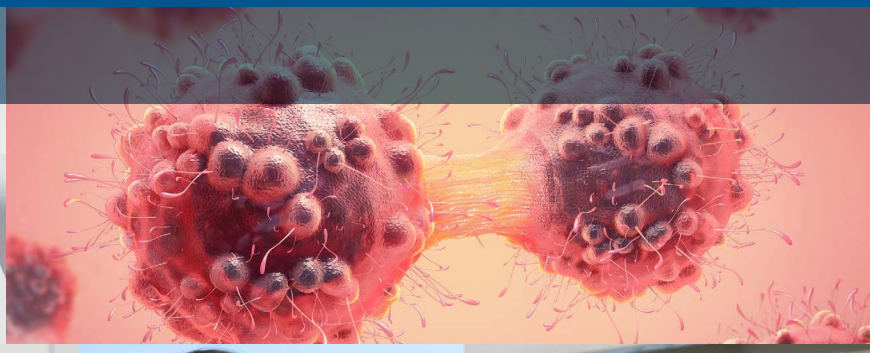
Agilent

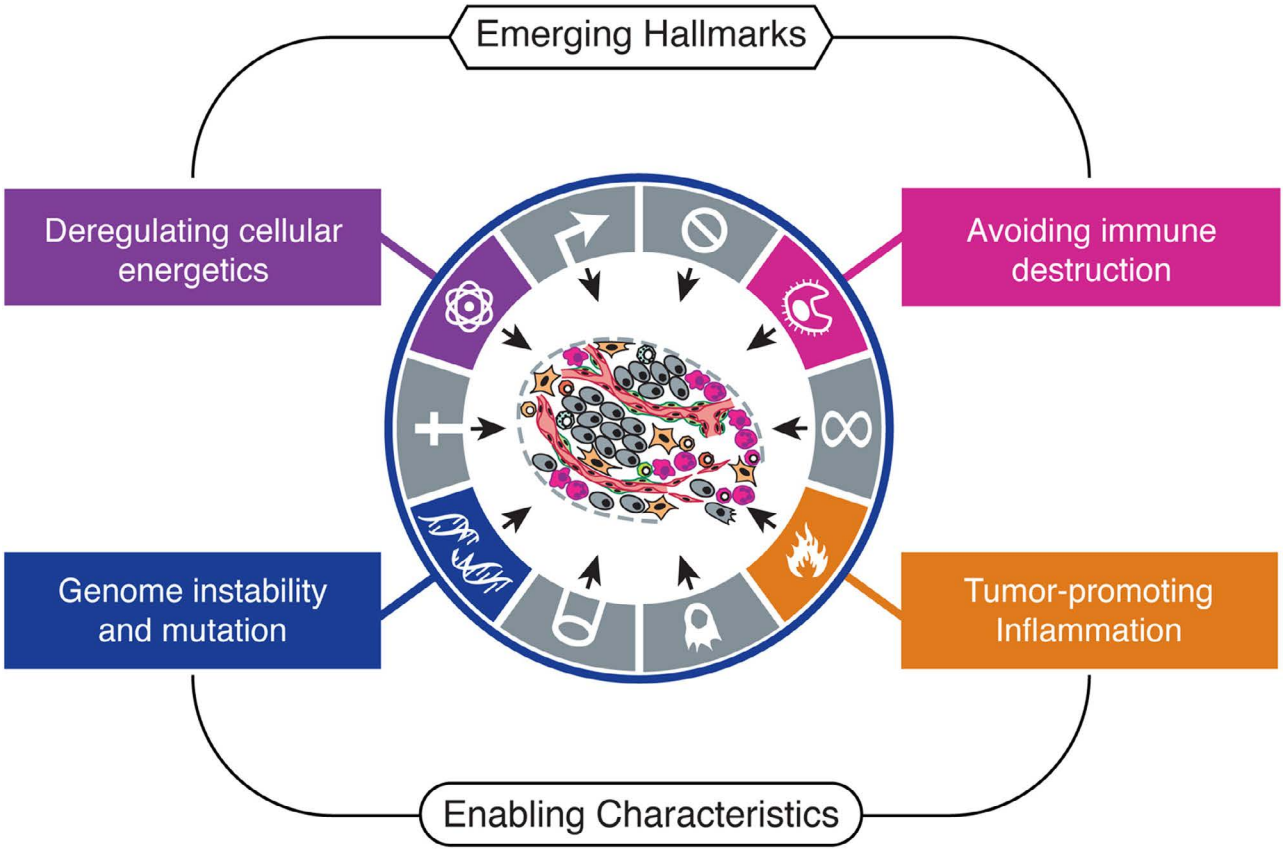
Trusted Answers

Agilent Seahorse XF Live-Cell Metabolism Solutions for Cancer Research



Metabolic reprogramming is a hallmark of cancer, and critical driver of all other hallmarks

Exploiting metabolic liabilities for therapeutic targeting



Cancer is a diverse collection of diseases linked to genetic changes that affect normal cell function, and metabolic reprogramming is emerging as a critical target in therapeutic intervention. Cancer cells are highly dependent on metabolic pathways to generate the necessary energy for many oncogenic processes -- rapid proliferation, survival, invasion, and metastasis – and will reprogram their metabolism to support these processes.

Today, researchers use a variety of cell-based assays such as gene and RNA expression, protein quantification, flow cytometry, and mass spectrometry -- to further their understanding of cancer biology. Investigating the dynamic nature of cellular metabolism and how cancer cells reprogram their metabolism to adapt and survive using *functional measurements in real-time* can reveal metabolic liabilities. These metabolic liabilities can then be exploited for therapeutic targeting.

Agilent Seahorse XF Cell Analysis solutions in cancer research

Generate functional measurements in real-time

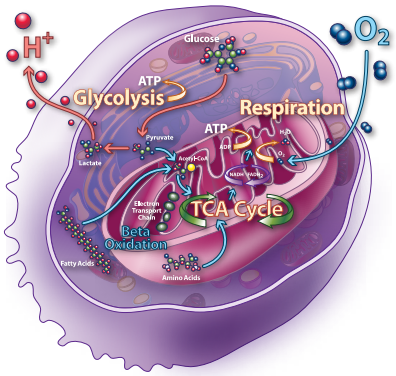
The Agilent Seahorse XF platform provides a direct measure of *simultaneous measurements of OXPHOS and glycolytic rate, in live cells, in real-time*. Using this technology, phenotypic evaluation of cancer cells in response to different metabolic substrates or inhibitors can be evaluated.

Agilent XF cell analysis features

- Live cell
- Real-time
- Label-free
- Dynamic injection ports
- Simultaneously measures oxygen consumption and glycolytic rates
- Provides quantitative glycolysis rates
- Measures quantitative ATP production rates

Discover why cancer researchers are using Agilent XF Cell Analysis technology to investigate:

- Metabolic drivers of oncogenic phenotypes
- Cancer cell malignancy & plasticity
- Substrate utilization in the tumor microenvironment
- Metabolic vulnerabilities to inform druggable target identification
- Cancer cell survival



Cancer cell dependencies and adaptation strategies go beyond glycolysis

Measure the variabilities in metabolic phenotypes driving cancer vulnerabilities

Cancer is a metabolic disease, which often characterized by a "Warburg effect" with upregulated glycolysis. However, metabolic phenotypes are substantially variable, and can serve as a critical predictor of cancer proliferation, vulnerabilities, and resistance to therapies. Agilent cell analysis provides a direct measure of functional live cell metabolism that illuminates cancer vulnerabilities driving cancer cell progression and proliferation.

Cancer metabolic phenotype and vulnerabilities are highly variable

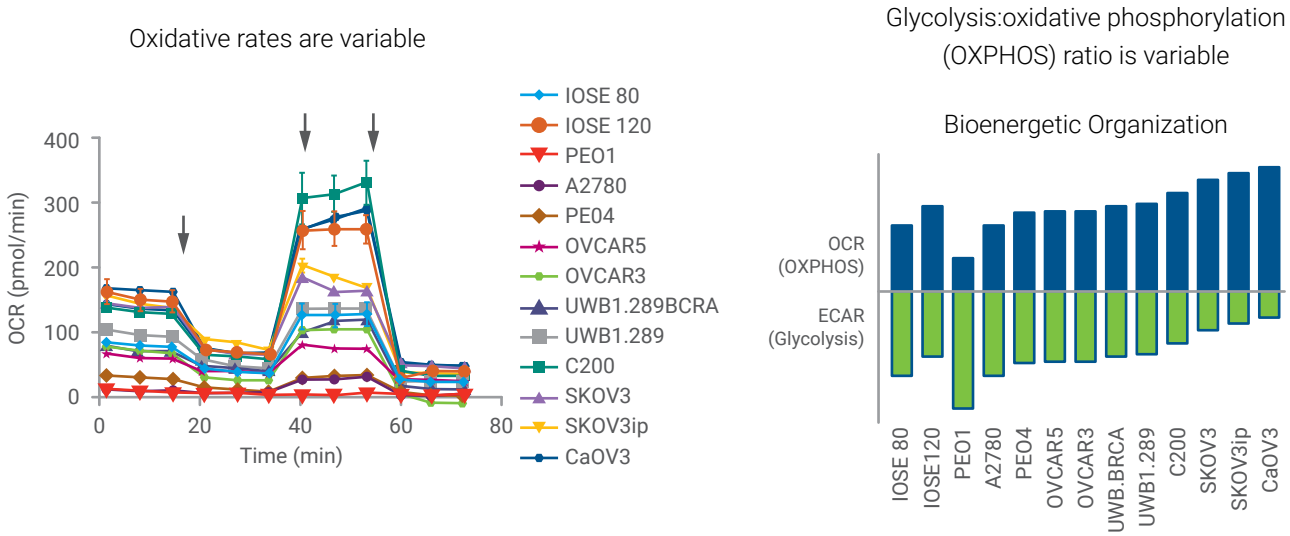


Figure 1. Cellular bioenergetic profiling of 13 ovarian cancer cell lines revealed significant bioenergetic diversity. Adapted from Dar, S., *et al.* Bioenergetic Adaptations in Chemoresistant Ovarian Cancer Cells. Sci Rep. 2017. 7 (1): 8760.

Cancer cells' metabolic profile reflects altered bioenergetic requirements to support proliferation

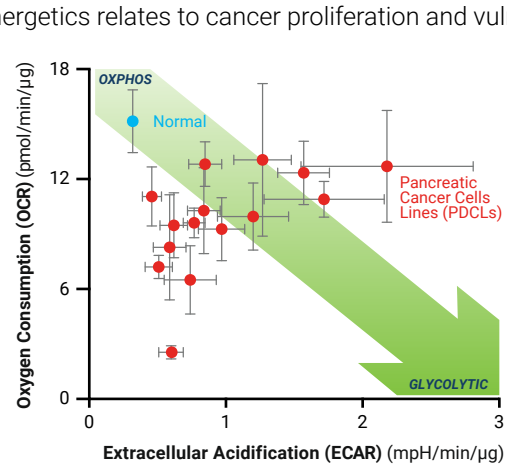


Figure 2. Pancreatic cancer cells switch to a glycolytic phenotype. Adapted from Hardie, R. A., *et al.* Mitochondrial mutations and metabolic adaptation in pancreatic cancer. Cancer Metab. 2017. 5 2.

Cancer cells are dynamic

Rapid changes in metabolism are a critical strategy in chemoresistance

Cancer proliferation is a rapid and dynamic process that demands significant biochemical energy. As a result, cancer cells exhibit an altered metabolism that may rely on one or both of the main metabolic pathways, glycolysis or oxidative phosphorylation. The ability of some cancer cells to switch between pathways is a key strategy driving cancer cell adaptation. Agilent cell analysis products enable simultaneous measurements of the two major metabolic pathways in live cells, in real-time.

Cancer cells rapidly exploit metabolism to adapt and survive through metabolic plasticity

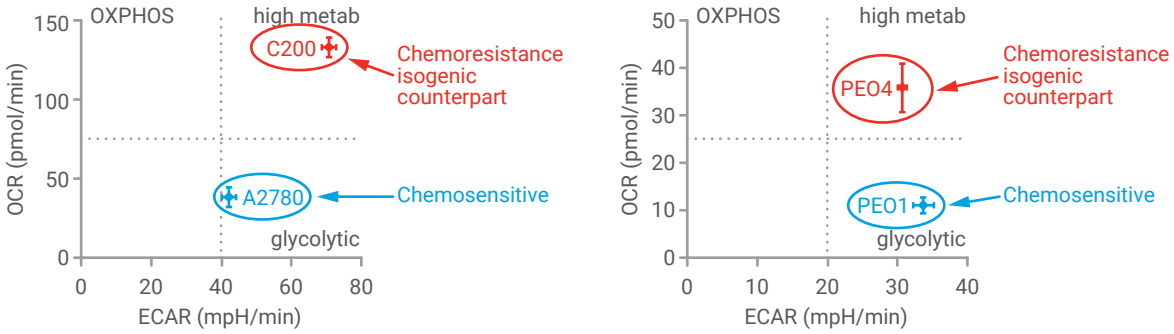


Figure 3. Chemosensitive ovarian cancer cell lines (A2780 and PEO1) displayed a glycolytic phenotype. In contrast, their chemoresistant isogenic counterparts (C200 and PEO4) exhibited a highly metabolically active phenotype with the ability to switch between oxidative phosphorylation or glycolysis (plasticity). Adapted from Dar, S., *et al.* Bioenergetic Adaptations in Chemoresistant Ovarian Cancer Cells. Sci Rep. 2017. 7 (1): 8760.

Metabolic vulnerabilities can reveal therapeutic targets for chemoresistance

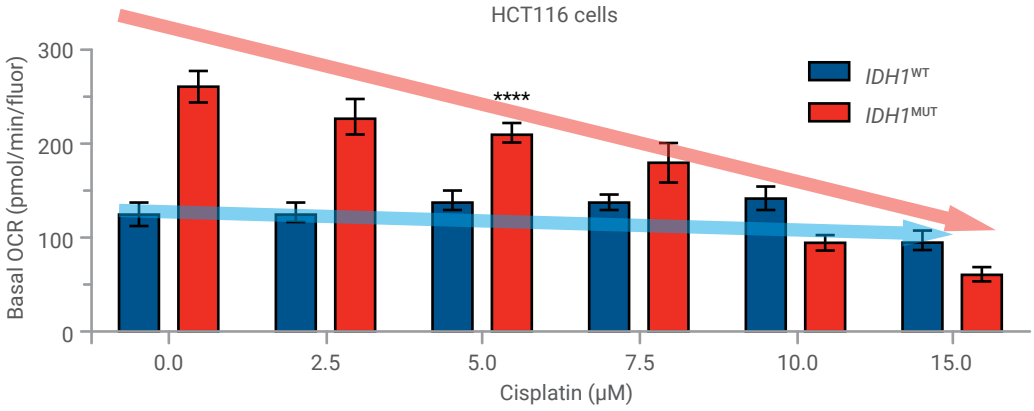


Figure 4. Agilent Seahorse XF analysis reveals that the increased chemosensitivity of cisplatin in IDH1MUT colon cancer cells is due to heightened vulnerability of oxidative phosphorylation metabolism. Cisplatin treatment in IDH1MUT HCT116 cells dose dependently decreased their oxygen consumption rate (OCR). Adapted from Khurshed, M., *et al.* IDH1-mutant cancer cells are sensitive to cisplatin and an IDH1-mutant inhibitor counteracts this sensitivity. FASEB J. 2018. fj201800547R.

Discover cancer cells' substrate dependencies

Cancer cells may alter lipid or amino acid metabolism, or shift the balance between anabolic and catabolic processes to adapt to the nutritional conditions of the tumor microenvironment. These processes may be analyzed directly via metabolic measurements.

Discover how Agilent cell analysis technology and metabolic phenotyping can provide a window into:

- Cellular dependencies, including fuels and microenvironment
- Metabolic vulnerabilities to inform druggable target identification
- Cancer drug development and efficacy

Agilent Seahorse XF technology reveals potential targets and mechanisms for antitumor and radiosensitizing drugs

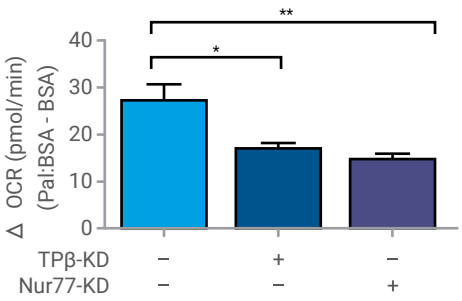


Figure 5. The Agilent Seahorse XF Analyzer reveals the critical role of Nur77 and TPb in melanoma cells adapting to fatty acid oxidation (FAO) under low glucose conditions. As FAO adaptation facilitates melanoma cell survival, Nur77 is implicated as a potential therapeutic target in melanoma. Adapted from Li, X. X., *et al.* Nuclear Receptor Nur77 Facilitates Melanoma Cell Survival under Metabolic Stress by Protecting Fatty Acid Oxidation. Mol Cell. 2018. 69 (3): 480-492 e7.

Agilent Seahorse XF technology differentiates the mechanisms of two lactate uptake inhibitors and antitumor drugs in whole cells and isolated mitochondria

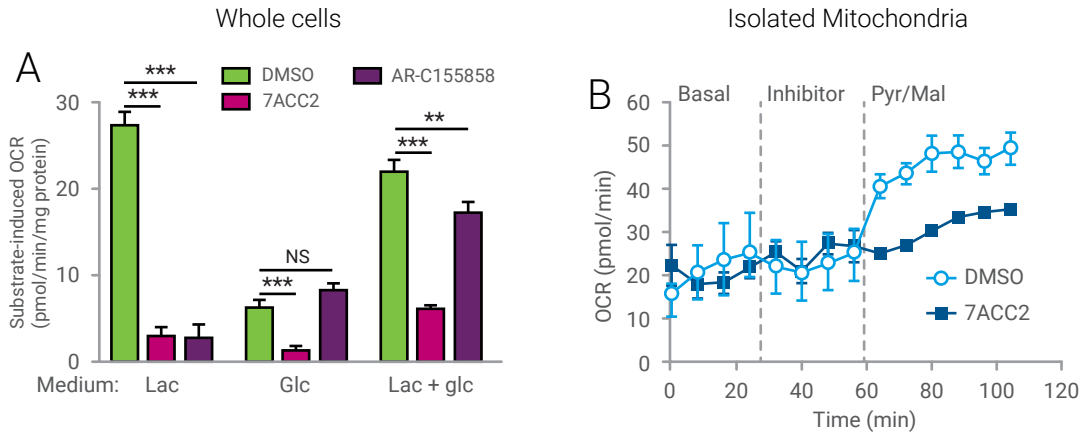
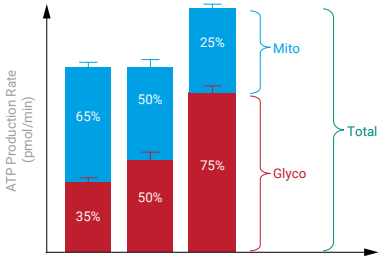
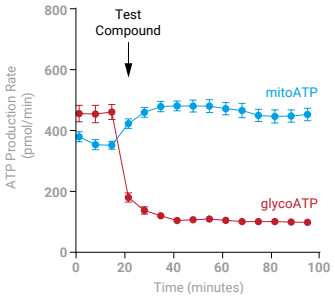


Figure 6. The Seahorse XF Analyzer first determined that, unlike lactate inhibitor AR-C155858, the compound 7ACC2 fulfills the tasks of blocking lactate use while preventing oxidative metabolism of glucose (6A, whole cervical cancer cells). Using isolated mitochondria, the Seahorse XF Analyzer further reveals that 7AAC2 works to inhibit lactate uptake via inhibition of the mitochondrial pyruvate carrier, which is a novel mechanism (6B, isolated mitochondria). Adapted from Corbet, C., *et al.* Interruption of lactate uptake by inhibiting mitochondrial pyruvate transport unravels direct antitumor and radiosensitizing effects. Nat Commun. 2018. 9 (1): 1208.

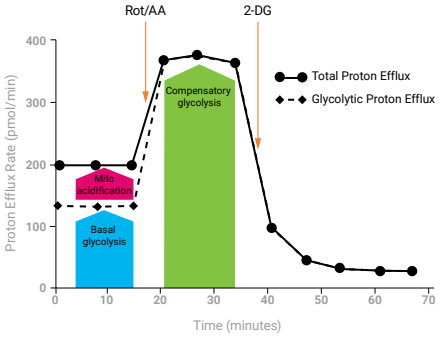
The gold standard assays for measuring cancer

Agilent Seahorse XF Real-Time ATP Rate Assay Kit
Cat No. 103592-100 (XF/XFe) & 103591-100 (XFp)



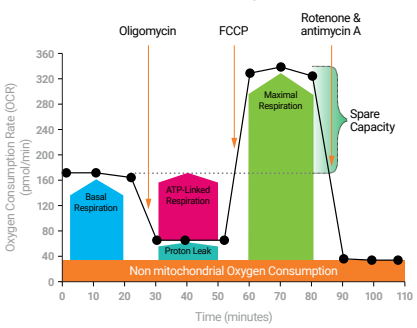


Agilent Seahorse XF Glycolytic Rate Assay Kit
Cat No. 103344-100 (XF/XFe) & 103346-100 (XFp)

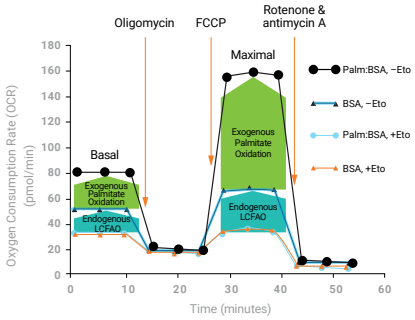


Discover cancer vulnerabilities, plasticity, and metabolic phenotyping with simultaneous measurements of oxidative phosphorylation and glycolysis, for a comprehensive picture of what is driving your cells function. *Now quantitative with the Agilent Seahorse XF Glycolytic Rate Assay and Real-Time ATP rate assay.*

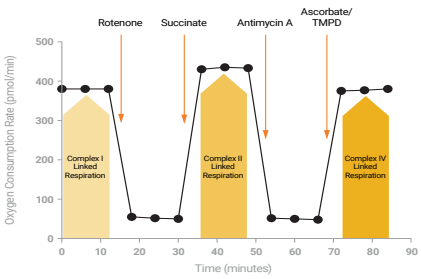
Agilent Seahorse XF Cell Mito Stress Test Kit
Cat No. 103015-100 (XF/XFe) & 103010-100 (XFp)



Agilent Seahorse XF Palmitate-BSA FAO Substrate Cat No. 102720-100



Agilent Seahorse XF Plasma Membrane Permeabilizer Cat No. 102504-100



Assess fuel and substrate utilization using the Agilent Seahorse XF Cell Mito Stress Test kit and Palmitate-BSA FAO substrate.

Perform the same assays you would perform on isolated mitochondria, without actually isolating mitochondria.

Agilent Seahorse XFe96 Analyzer

Seahorse XF real-time assays provide the tools for studying dependencies, oncogenes, therapeutic targeting, and more.

Model the tumor microenvironment:

- Agilent Seahorse XFe24 and XFe96 Analyzers are compatible with a hypoxia chamber
- The Seahorse XFe96 Analyzer provides a spheroid-3D option

Agilent Cell Analysis Portfolio

Our market leading technologies in real-time live cell analysis have helped researchers push new boundaries across a number of research areas. Learn about our complete portfolio of solutions by visiting our website at **www.agilent.com/chem/discoverxf**

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Published in the USA, May 20, 2019
5994-0741EN

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