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冷泉港生物科技股份有限公司
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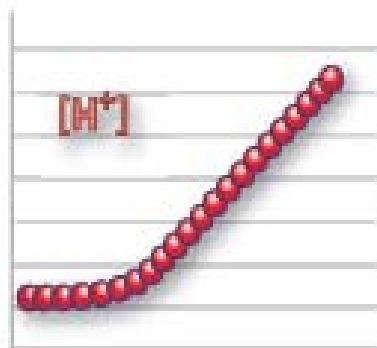


Seahorse Bioscience

A Better Option: Real-Time Cell Metabolism in a Microplate



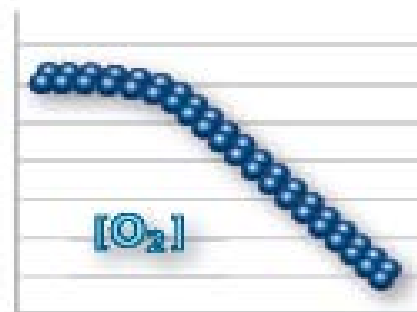
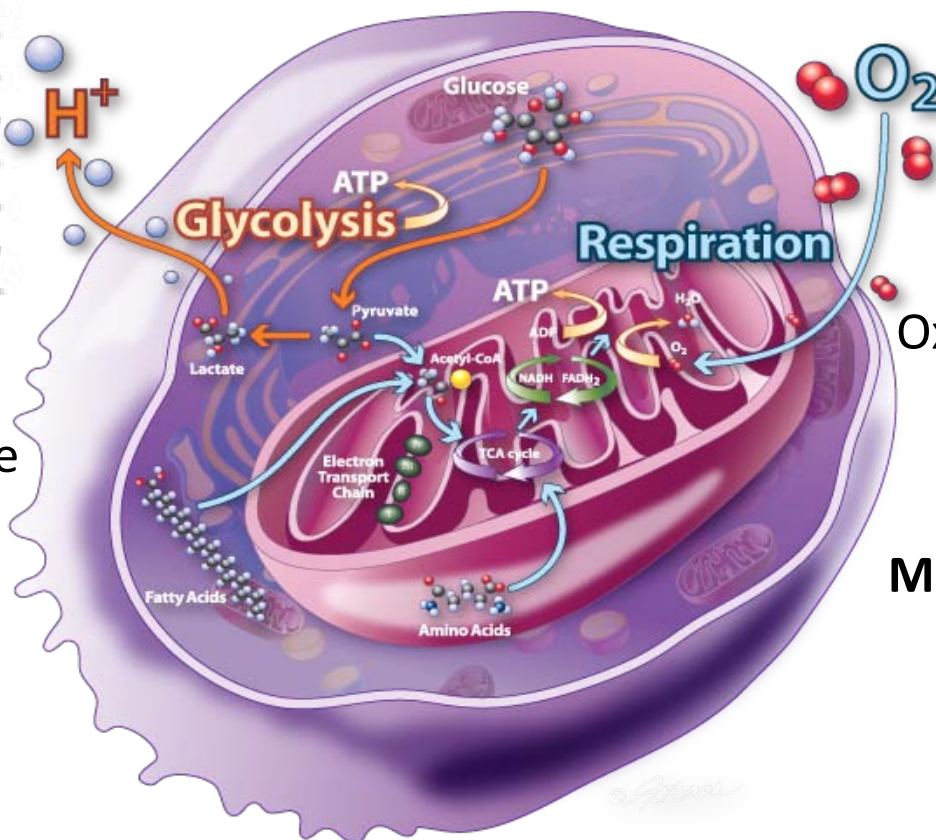
XF^e Analyzers Measure the Two Major Energy Pathways



Extracellular acidification rate
(ECAR)

=

Glycolysis

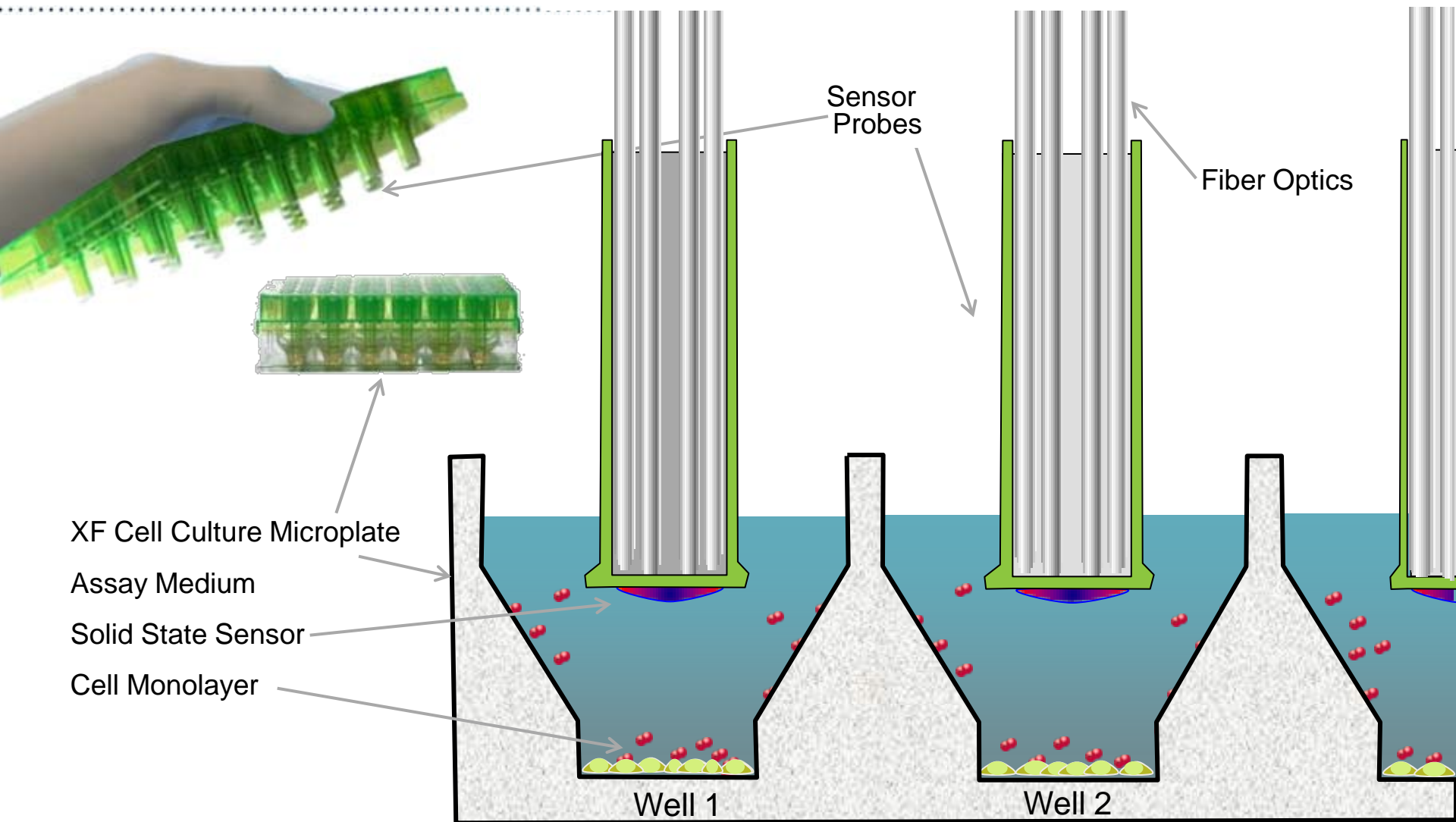


Oxygen Consumption Rate
(OCR)

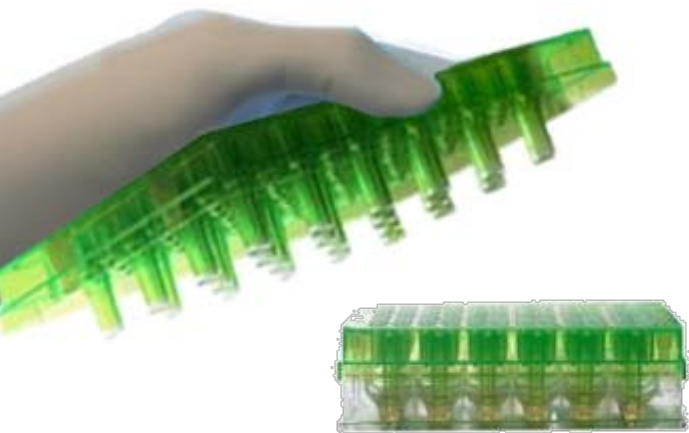
=

Mitochondrial Respiration

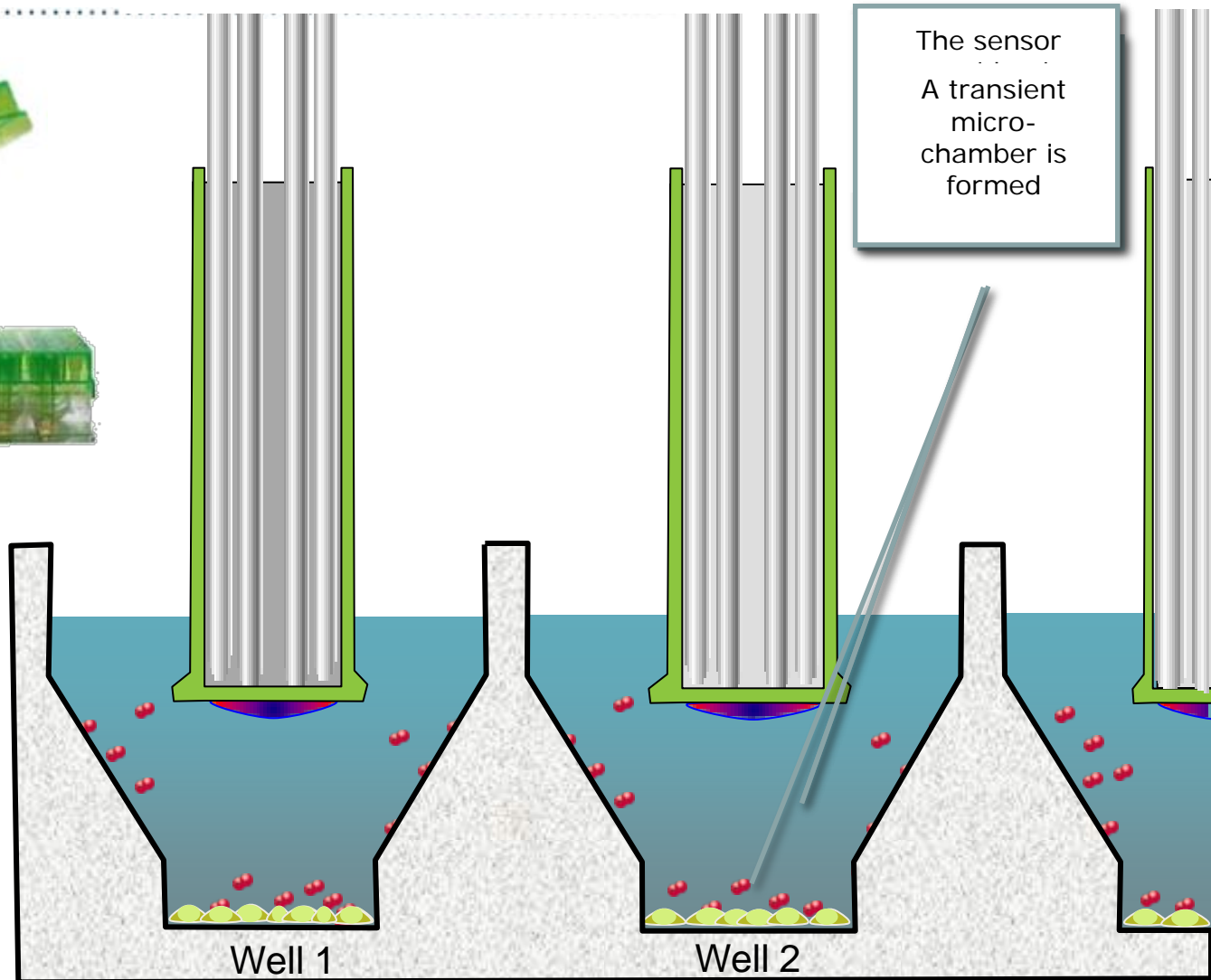
Measuring Mitochondrial Respiration and Glycolysis in a Microplate



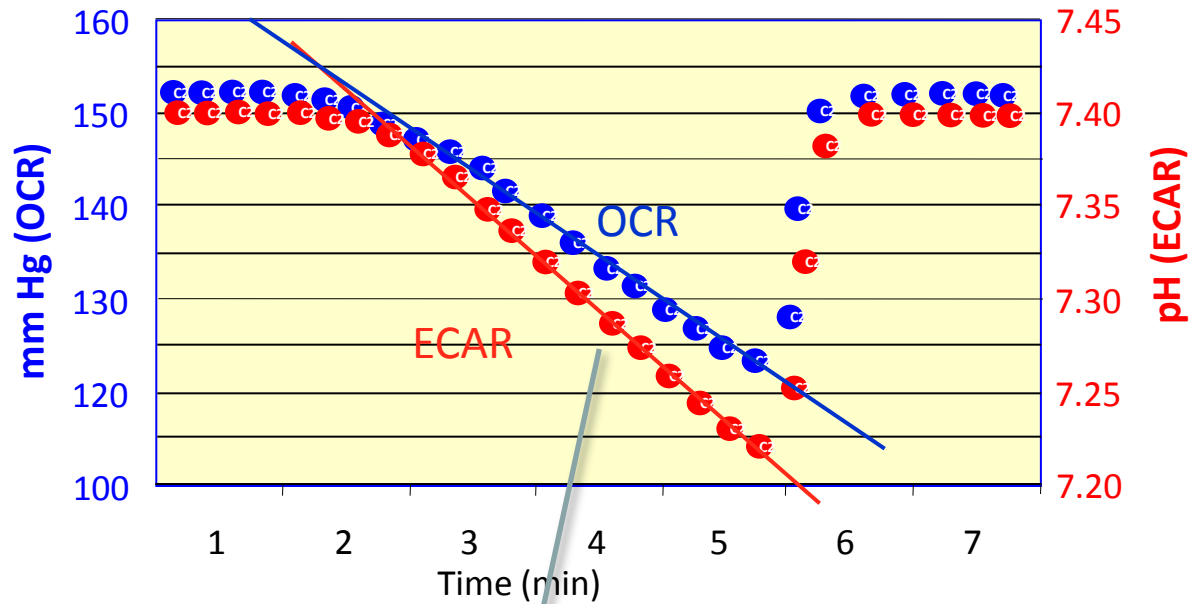
Measuring Mitochondrial Respiration and Glycolysis in a Microplate



The transient micro-chamber enables rapid measurement of mitochondrial respiration and glycolysis in minutes

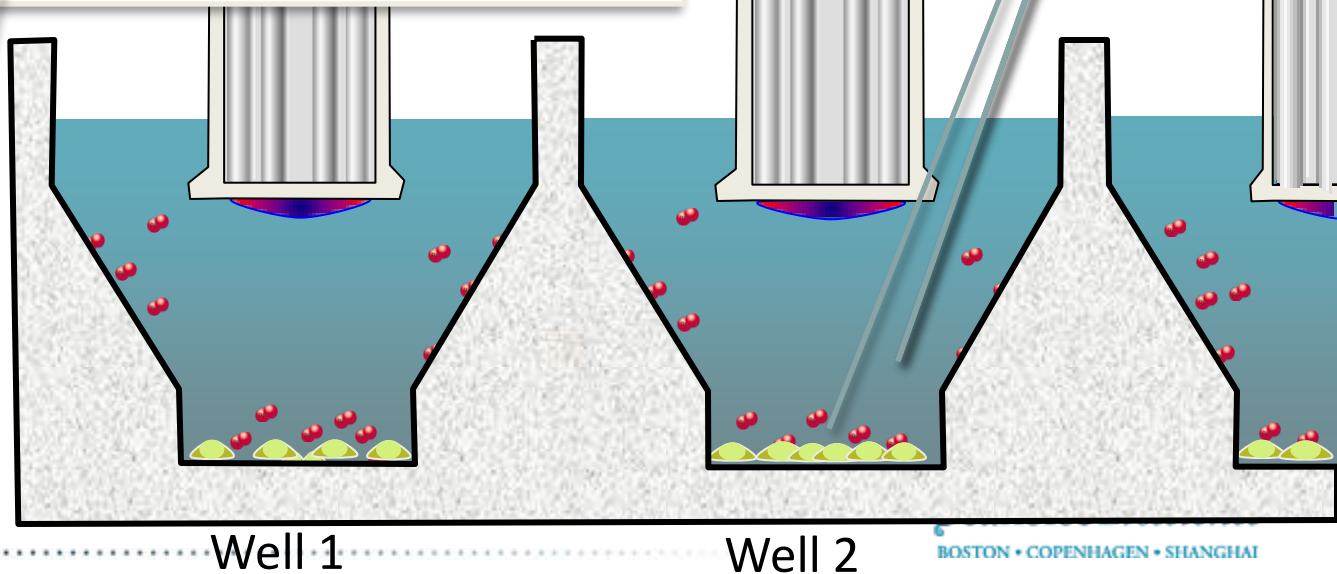


Metabolism in a Microplate- Cellular bioenergetics for the 21st century



The rate is calculated from the slope

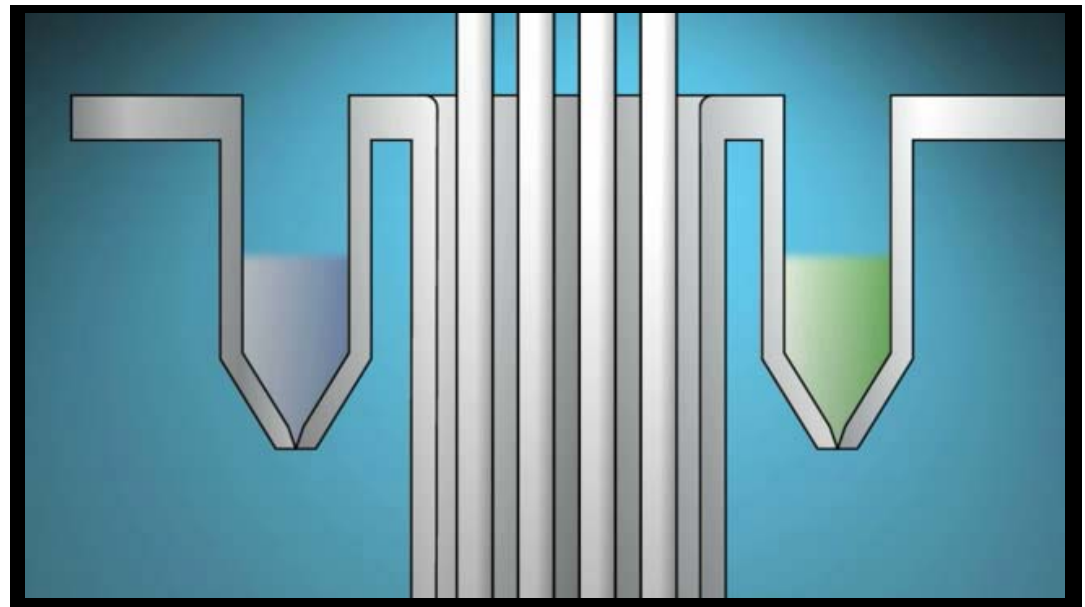
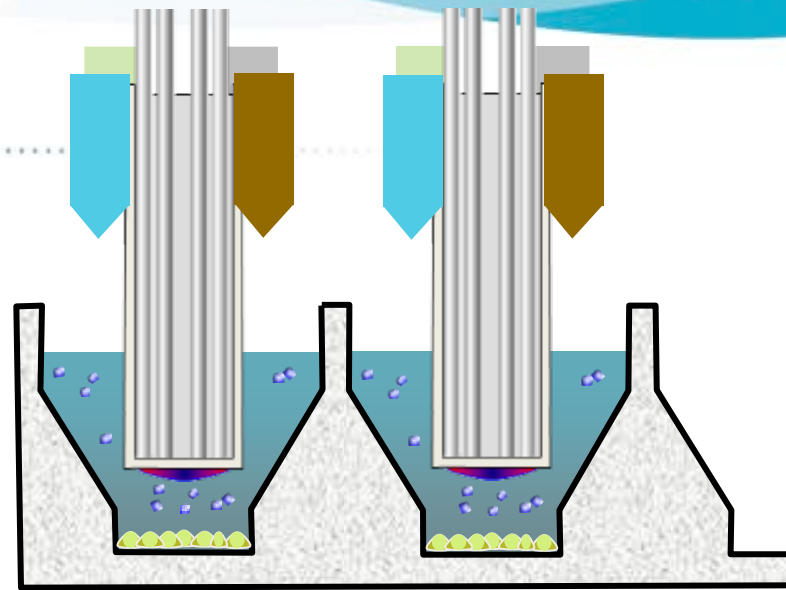
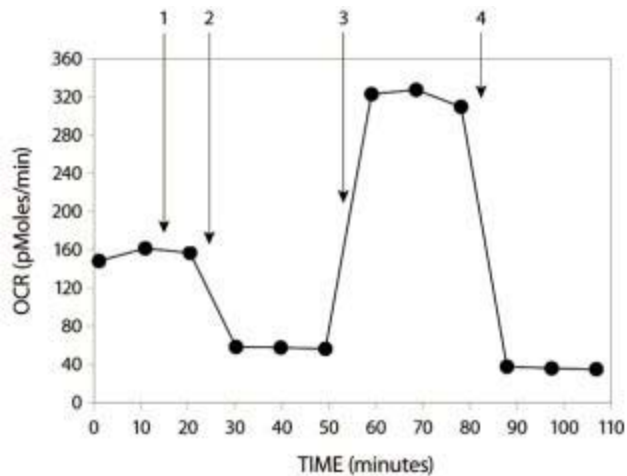
The bio-cartridge is raised, bringing the system back to baseline



Automated Drug Injection Ports Enable Kinetic, Functional Data



- 4 drug injection ports per well
- Add inhibitors, stimulants, substrates, and compounds
- Injections are defined by the user





What is making XF Analyzer unique for scientists

- ◆ Platform to simultaneously measure two parameters (OCR and ECAR)
- ◆ Rapid, real-time and label-free technology
- ◆ Microplate format and high throughput
- ◆ Wide kinds of cells: Assays adherent cells, suspension cells and subcellular components
- ◆ Up to four injection ports
- ◆ Sensitive and precision optical microsensor detection system
- ◆ Intuitive software with touch screen interface and data analysis system

Seahorse XF Extracellular Flux Analyzers, FluxPaks & Kits

XF^e 24细胞代谢分析仪



XF^e 96细胞代谢分析仪



XF测试样品制备仪



XF96 & XF24 FluxPaks



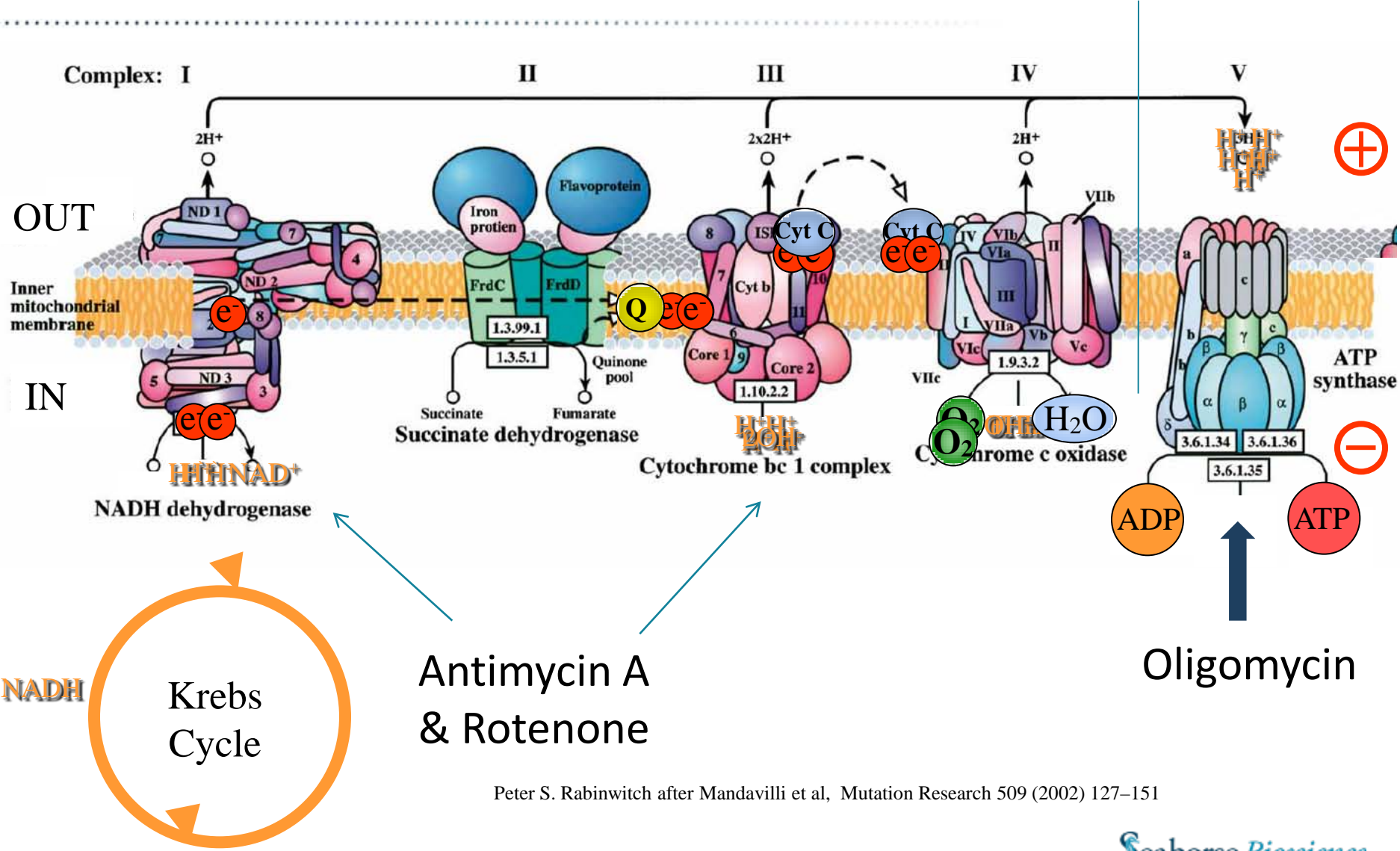
XF Stress Test Kits & Reagents



Application



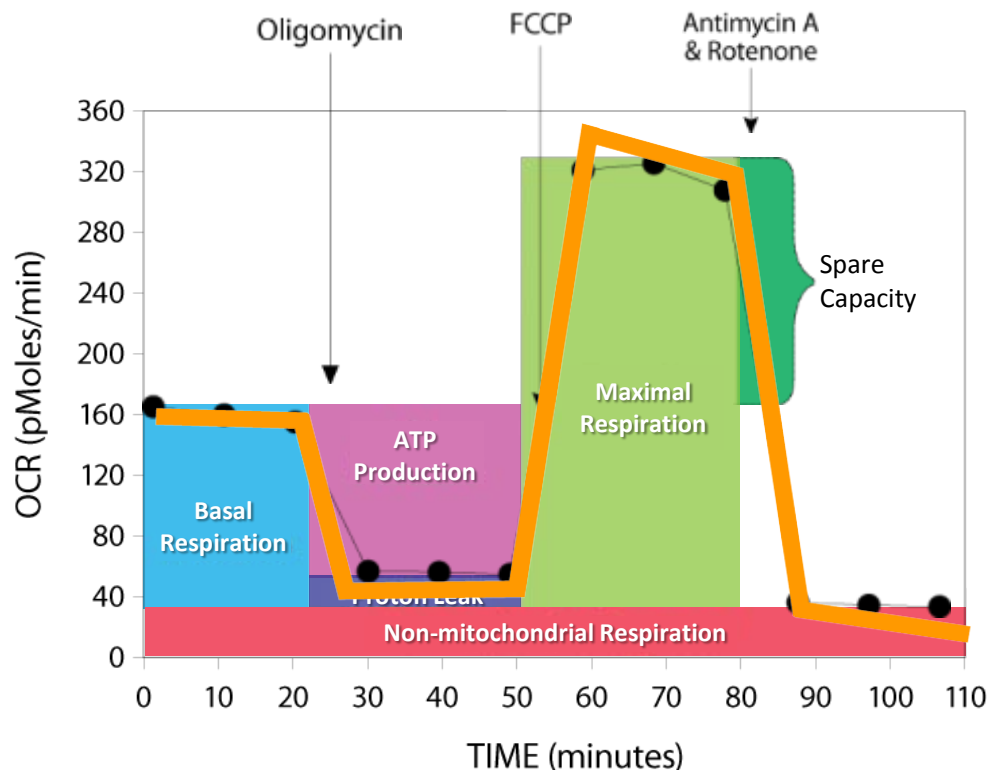
Mitochondrial Electron Transport Chain



Peter S. Rabinwitch after Mandavilli et al, Mutation Research 509 (2002) 127-151

XF CELL MITO STRESS TEST

The Gold Standard That Makes You a Bioenergetics Expert



XF Cell Mito Stress Test Profile

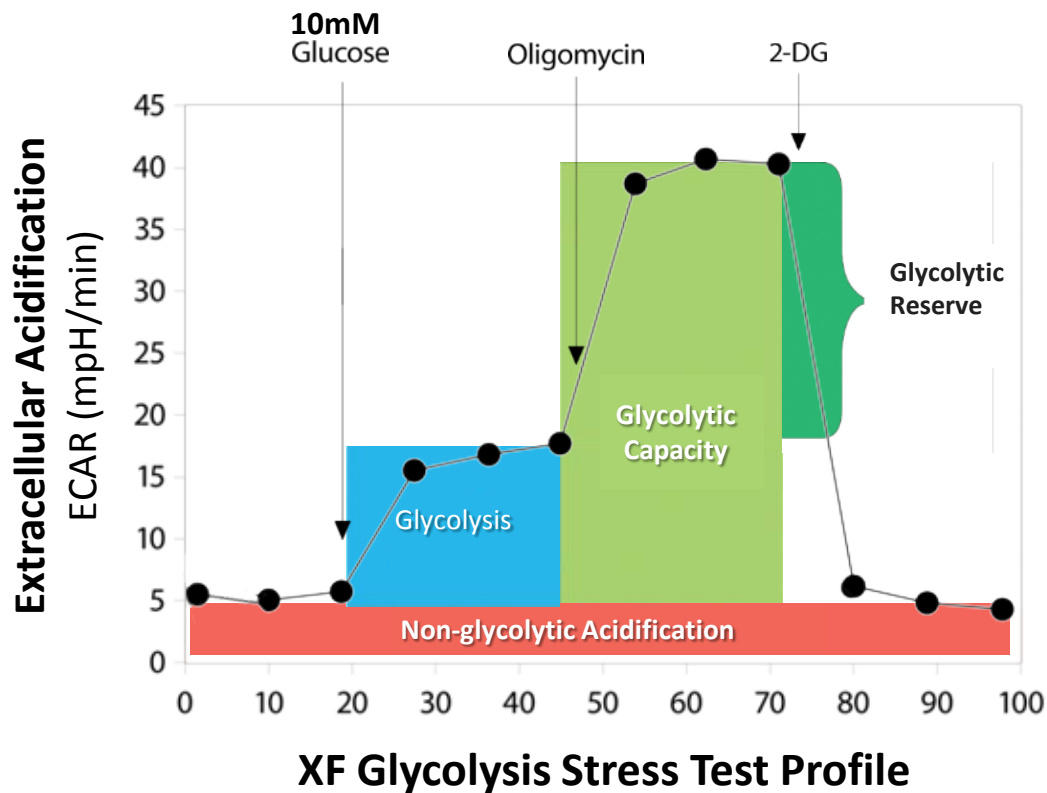
Kit measures the key parameters of mitochondrial function:

- Basal Respiration
- ATP Production
- Maximal and Spare Capacity
- Proton Leak



XF GLYCOLYSIS STRESS TEST

XF Glycolysis Stress Test Kit

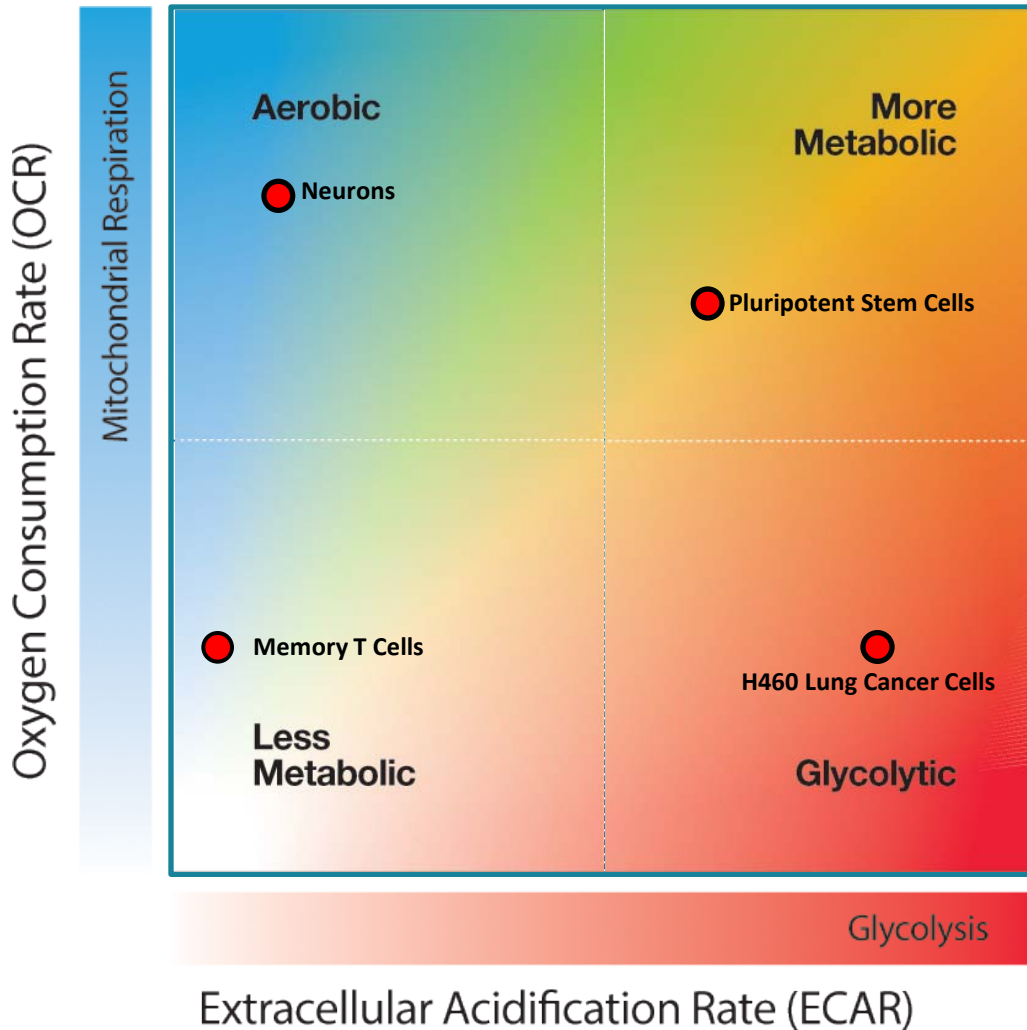


Measures the key parameters of glycolytic function:

- Non-glycolytic Acidification
- Glycolysis
- Glycolytic Capacity
- Glycolytic Reserve



XF^e Metabolic Phenotype Assay - PhenoGram



Measures the metabolic state of cells:

- Less Metabolic
- Aerobic
- Glycolytic
- More Metabolic

Warburg Effect

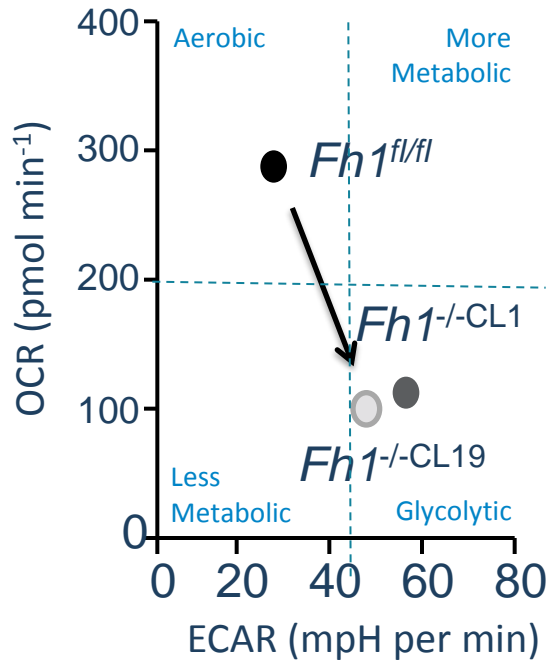
Reverse Warburg Effect

Crabtree Effect

Pasteur Effect

XF^e Assays Measure Metabolic Switching (Cancer, Diabetes and Obesity)

Gene Induced

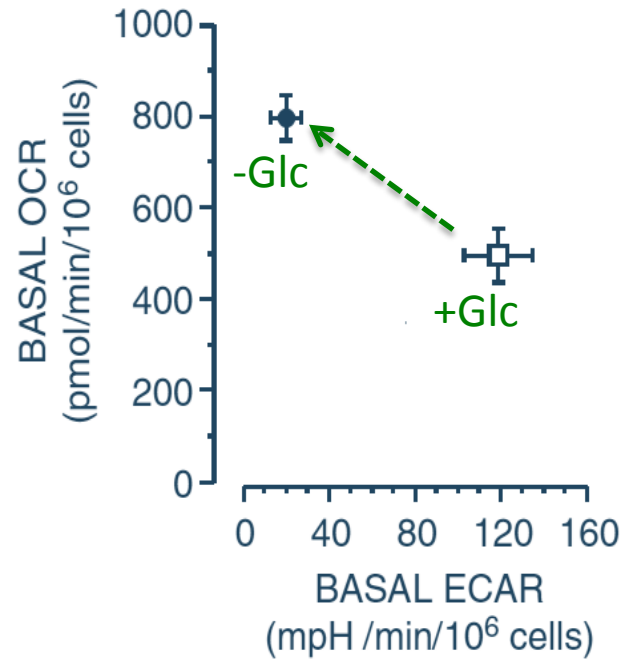


Kidney epithelial cells +/- fumarate hydratase

Haem oxygenase is synthetically lethal with the tumour suppressor fumarate hydratase.

Frezza *et al.* Nature. 2011 Aug 17;477(7363):225-8.

Substrate Induced

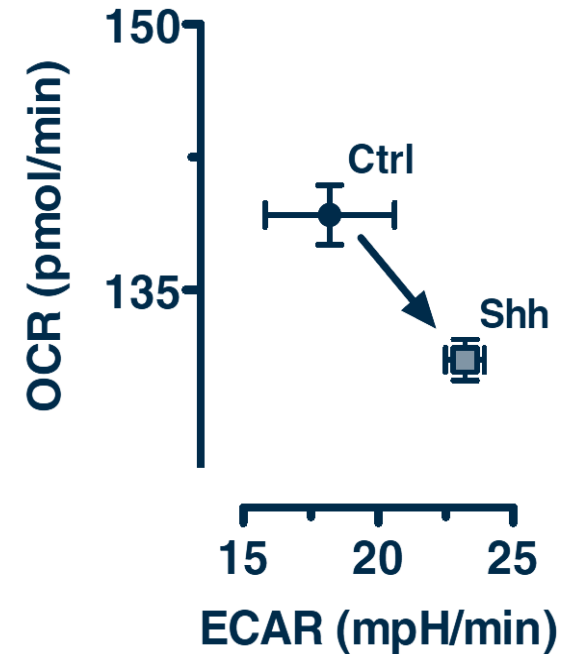


Mantle cell lymphoma cells +/- glucose

Switching from aerobic glycolysis to oxidative phosphorylation modulates the sensitivity of mantle cell lymphoma cells to TRAIL.

Robinson *et al.* Oncogene. 2012 Nov 29;31(48):4996-5006.

Signaling Pathway Induced

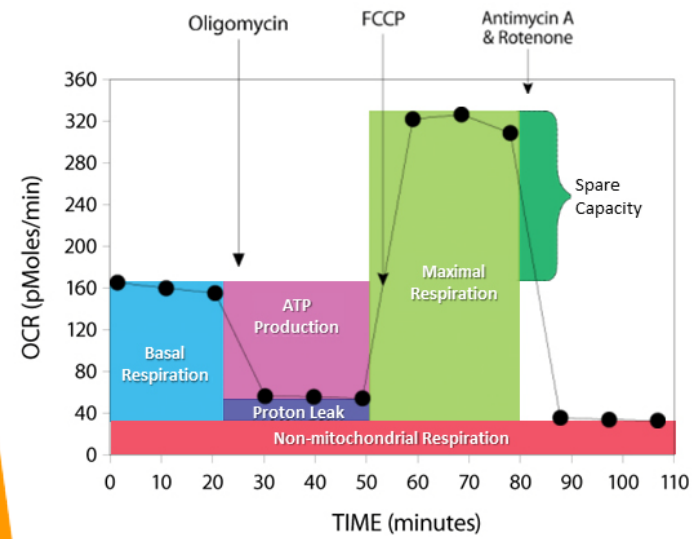


Adipocytes +/- Hedgehog ligand

Hedgehog partial agonism drives Warburg-like metabolism in muscle and brown fat.

Teperino R, *et al.*, Cell. 2012 Oct 12;151(2):414-26.

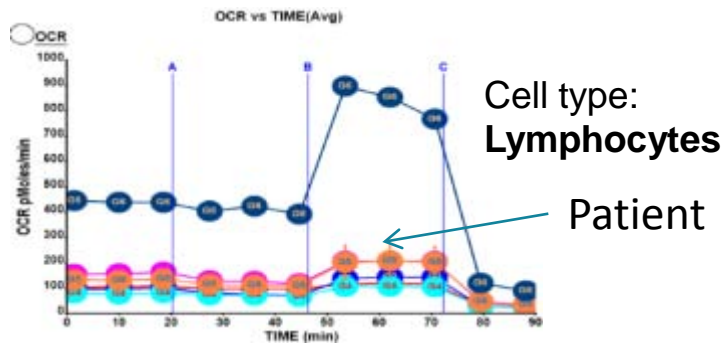
Seahorse Simplifies Measuring Cellular Metabolism



XF Cell Mito Stress Test Profile

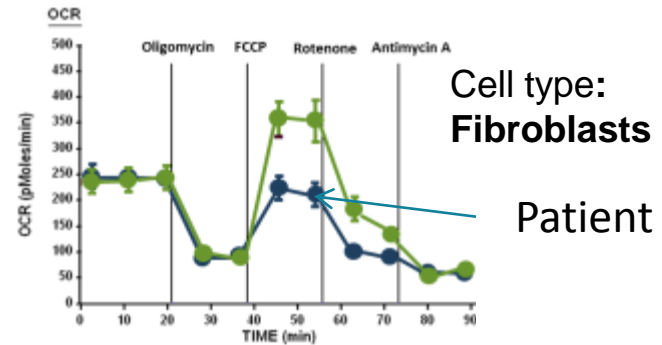
TRANSLATIONAL MEDICINE

Stress Test Identifies Mitochondrial Dysfunction in Diseases



HIV *

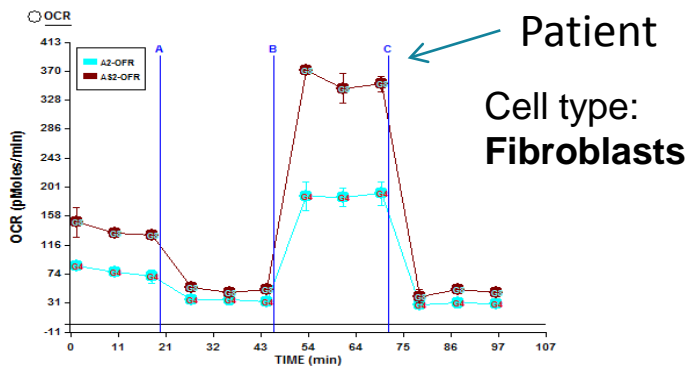
↓ Lower spare capacity in patients



Parkinson's Disease

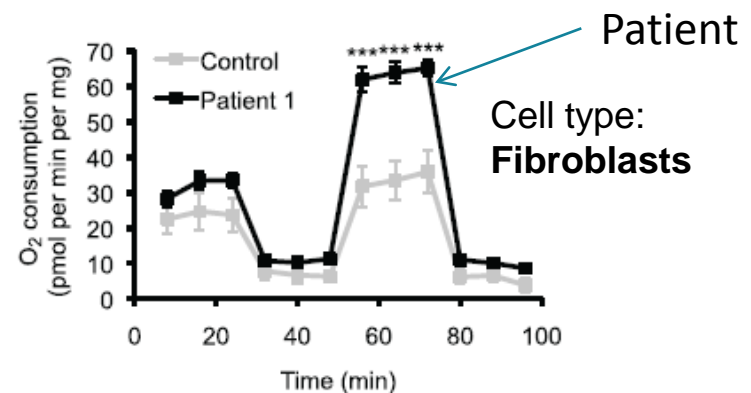
↓ Lower spare capacity in patient

Data courtesy of James Bennet Lab
University of Virginia



Autism *

↑ Higher spare capacity in patient



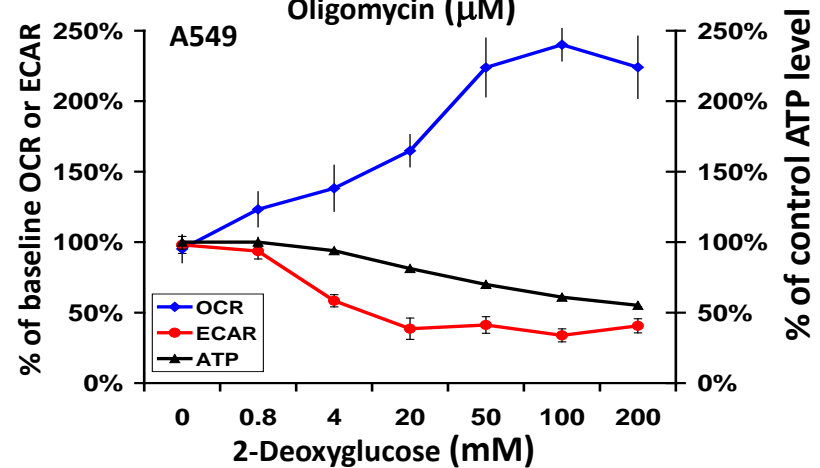
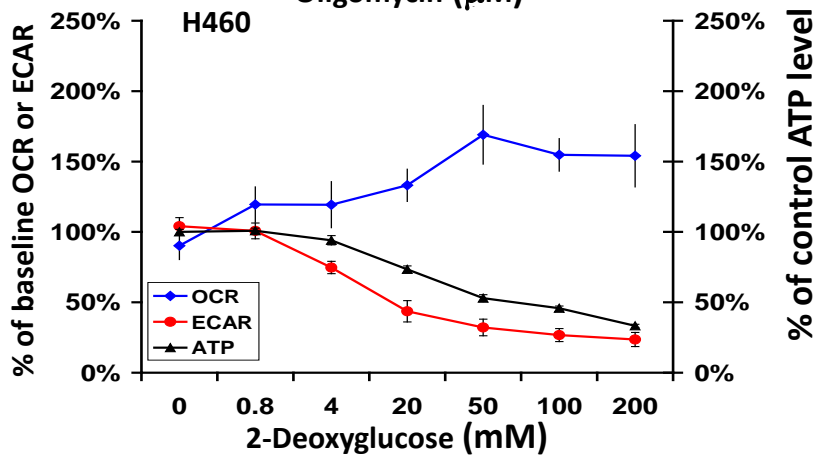
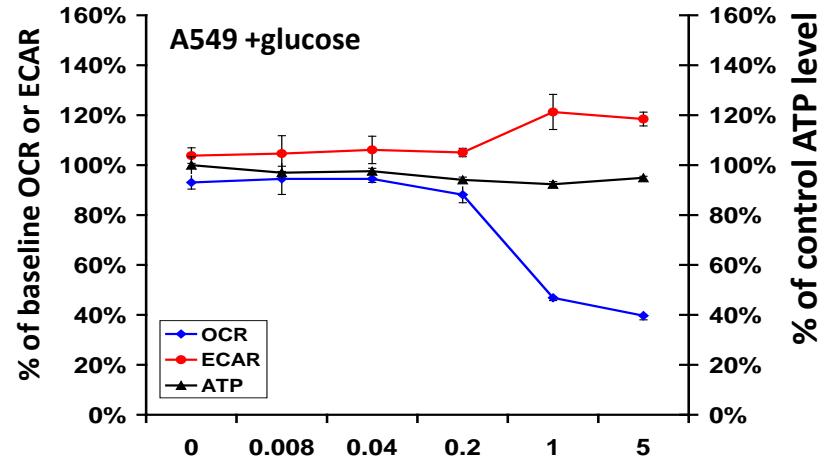
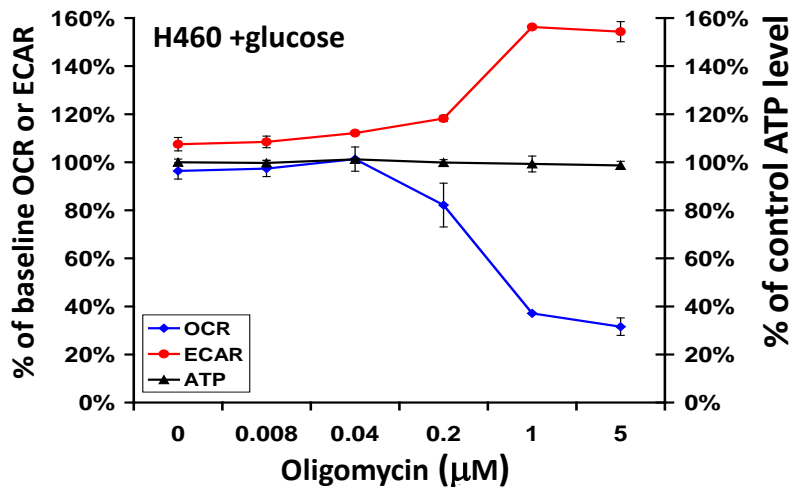
Multiple acyl-CoA dehydrogenase deficiency (MADD) **

↑ Higher spare capacity in patient

Data courtesy of Dr. Pinar Coskun,
Department of Neurobiology and Behavior at UC Irvine

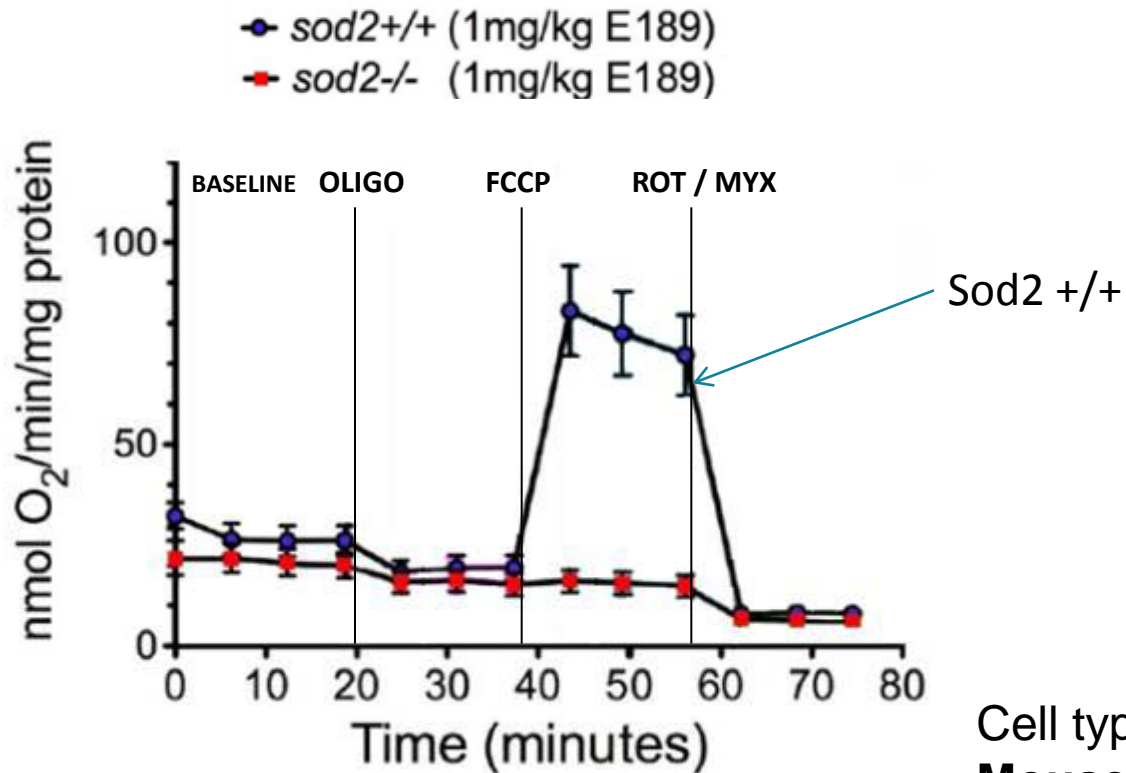
PLoS One. 2009 Dec 17; 4(12):e8329.
Song Y et al

High Glycolytic Capacity and Impaired Oxidative Phosphorylation in Tumor cells



NEURODEGENERATION

Spare Capacity Reveals More Than Basal Metabolism



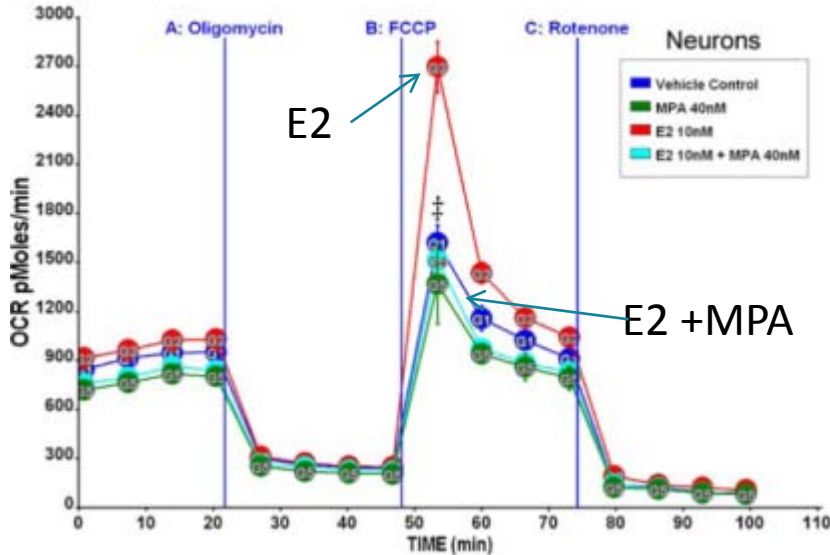
Cell type:
Mouse CD-1
Synaptosomes

Free Radic Biol Med. 2011 Apr 1; 50(7):866-873.

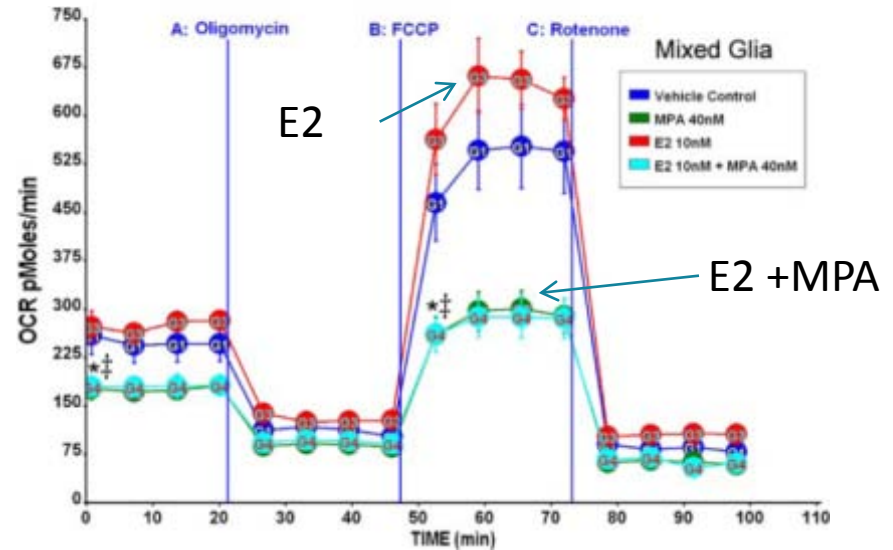
Impaired spare respiratory capacity in cortical synaptosomes from Sod2 null mice

Flynn J M, Choi S W, Day N U, Gerencser AA, Hubbard A and Melov S

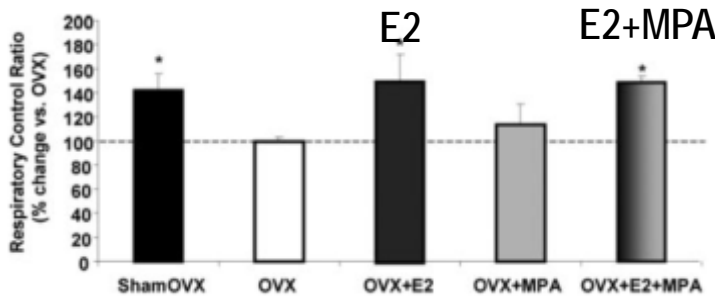
Stress Test Reveals Link Between Cytosol and Hormone Therapy in Primary Neurons and Mixed Glia



Primary rat hippocampal neurons



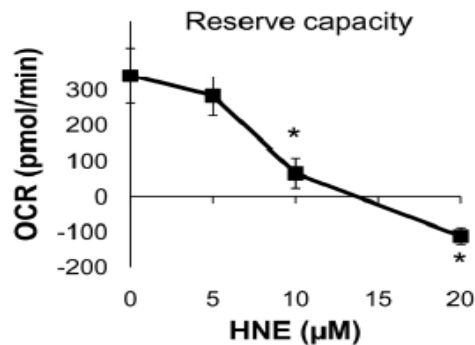
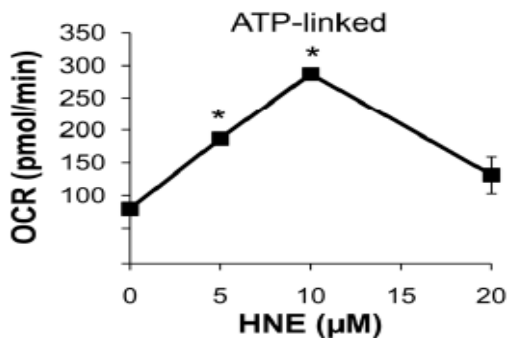
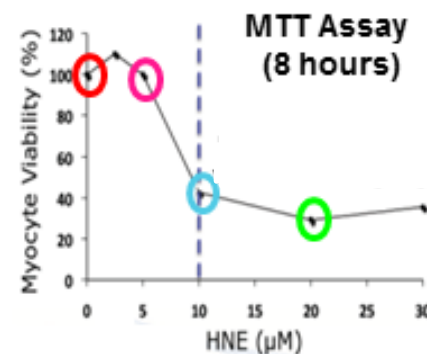
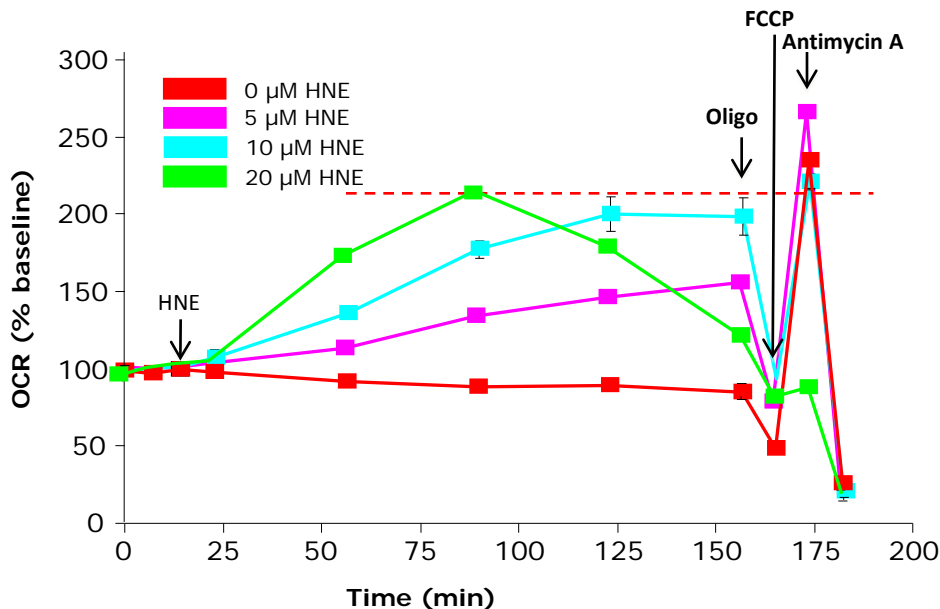
Primary rat mixed glia



reduces the protective effect of estrogen [E2] in neurons and mixed glia whole rat brain mitochondria

Stress Test Sensitivity Reveals Sub-Lethal Stress Response and Mechanism

XF Cell Mito Stress Test



Cell type:
**Neonatal Rat
Ventricular
Myocytes**

Biochem J. 2009 Nov 15;425(1):99-107

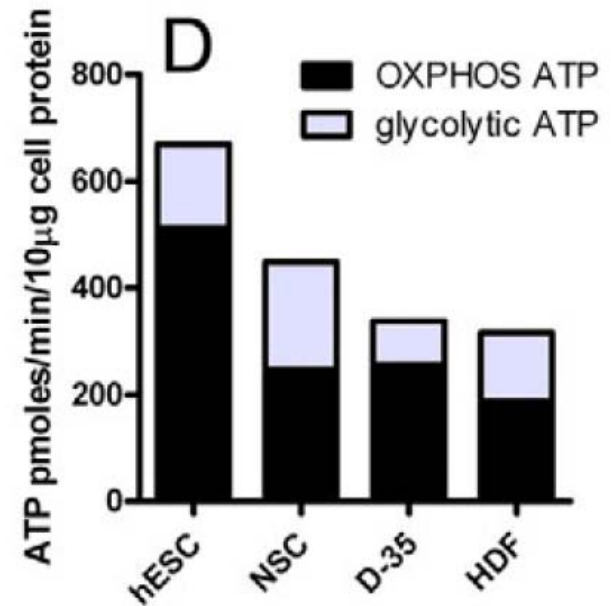
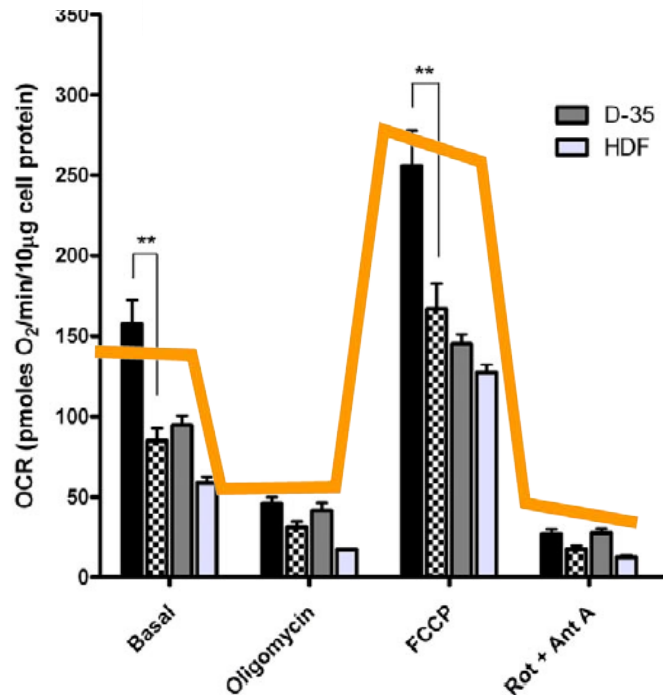
Importance of the bioenergetic reserve capacity in response to cardiomyocyte stress induced by 4-hydroxynonenal

Bradford G. Hill, Brian P. Dranka, Luyun Zou, John C. Chatham and Victor M. Darley-Usmar

STEM CELLS

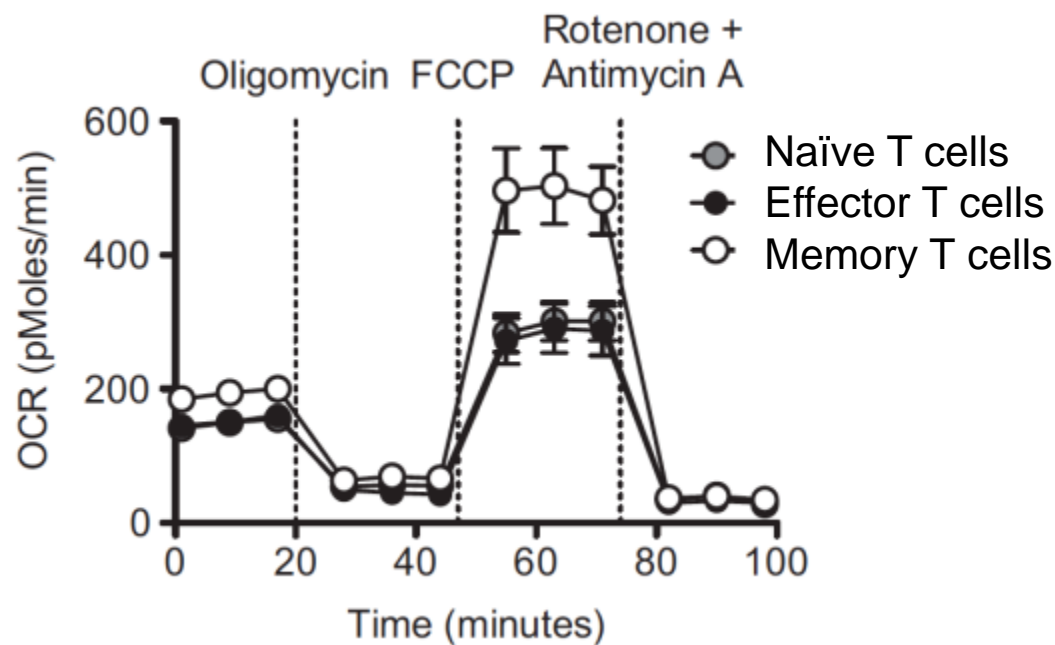
Stress Test Reveals Differentiation Status

- hESC Pluripotent I6 human embryonic stem cells
- ▣ NSC Multipotent I6 neural stem cells
- D-35 Differentiated I6 neural stem cells
- HDF BJ fibroblasts

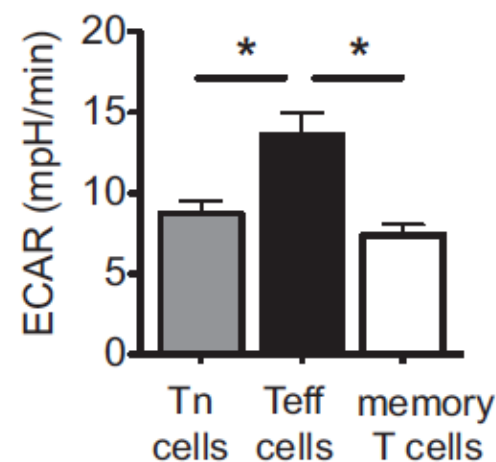


Human embryonic stem cells have higher levels of mitochondrial respiration and a greater proportion of ATP production through mitochondrial respiration

Spare Capacity Affects Memory T Cell Development and Survival

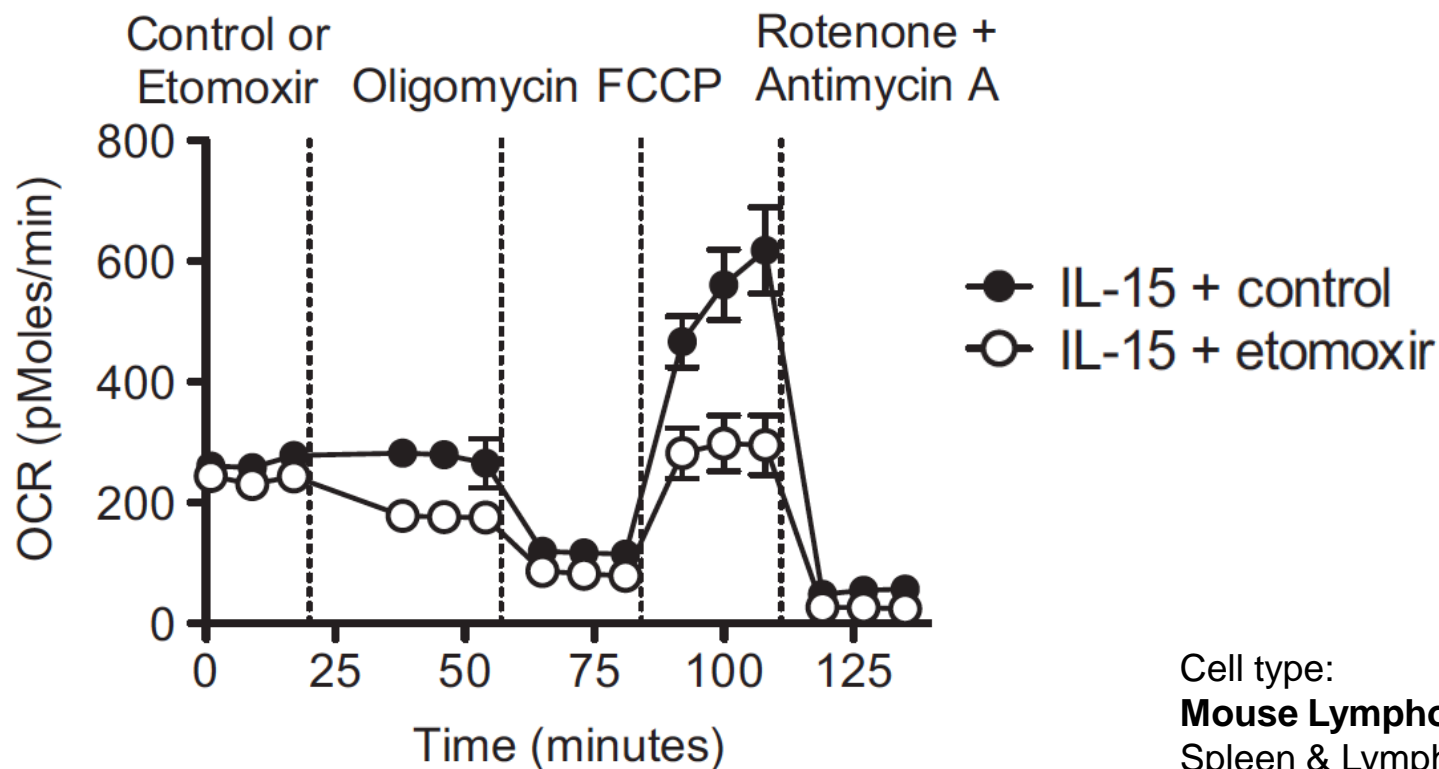


B



Cell type:
Mouse Lymphocytes
 Spleen & Lymph Nodes

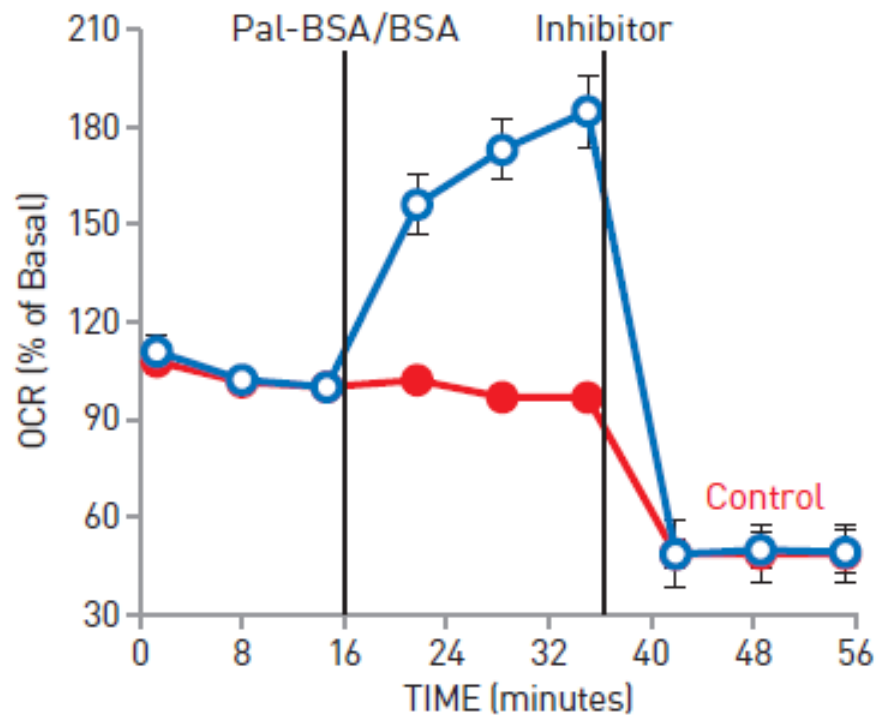
Spare Capacity in CD8+ T Cells is Dependent on Mitochondrial Fatty Acid Oxidation



Cell type:
Mouse Lymphocytes
 Spleen & Lymph Nodes
 Fatty acid source is FBS

XF FAO Kit

XF Palmitate-BSA FAO Reagent



Provides the first fully validated and standardized Palmitate-BSA FAO reagent:

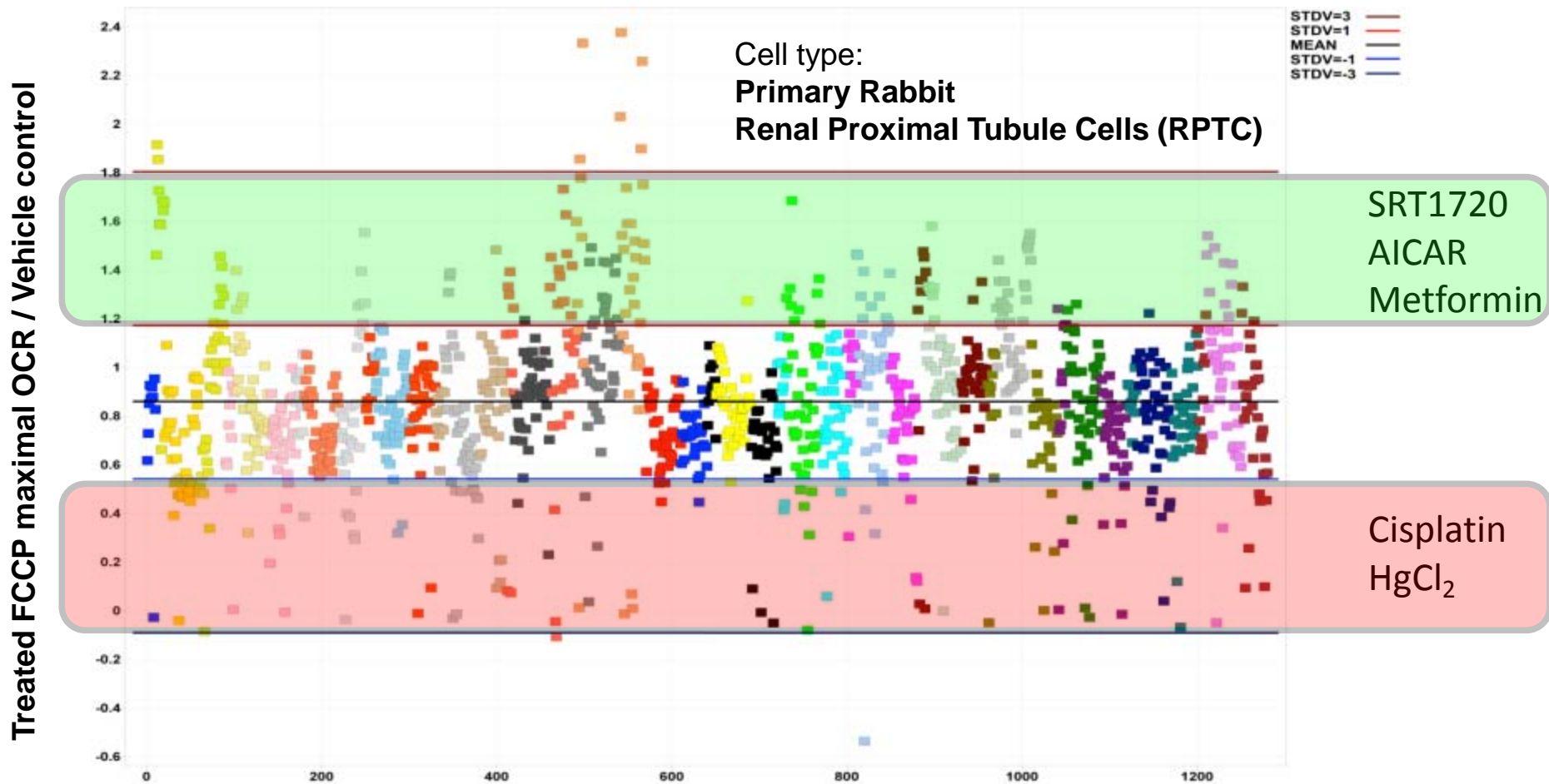
- No substrate preparation
- Activity tested
- Quality controlled



SCREENING

Drug Discovery and Toxicity

Results from first pass screen of LOPAC library (1,280) for mitochondrial biogenesis and toxicity



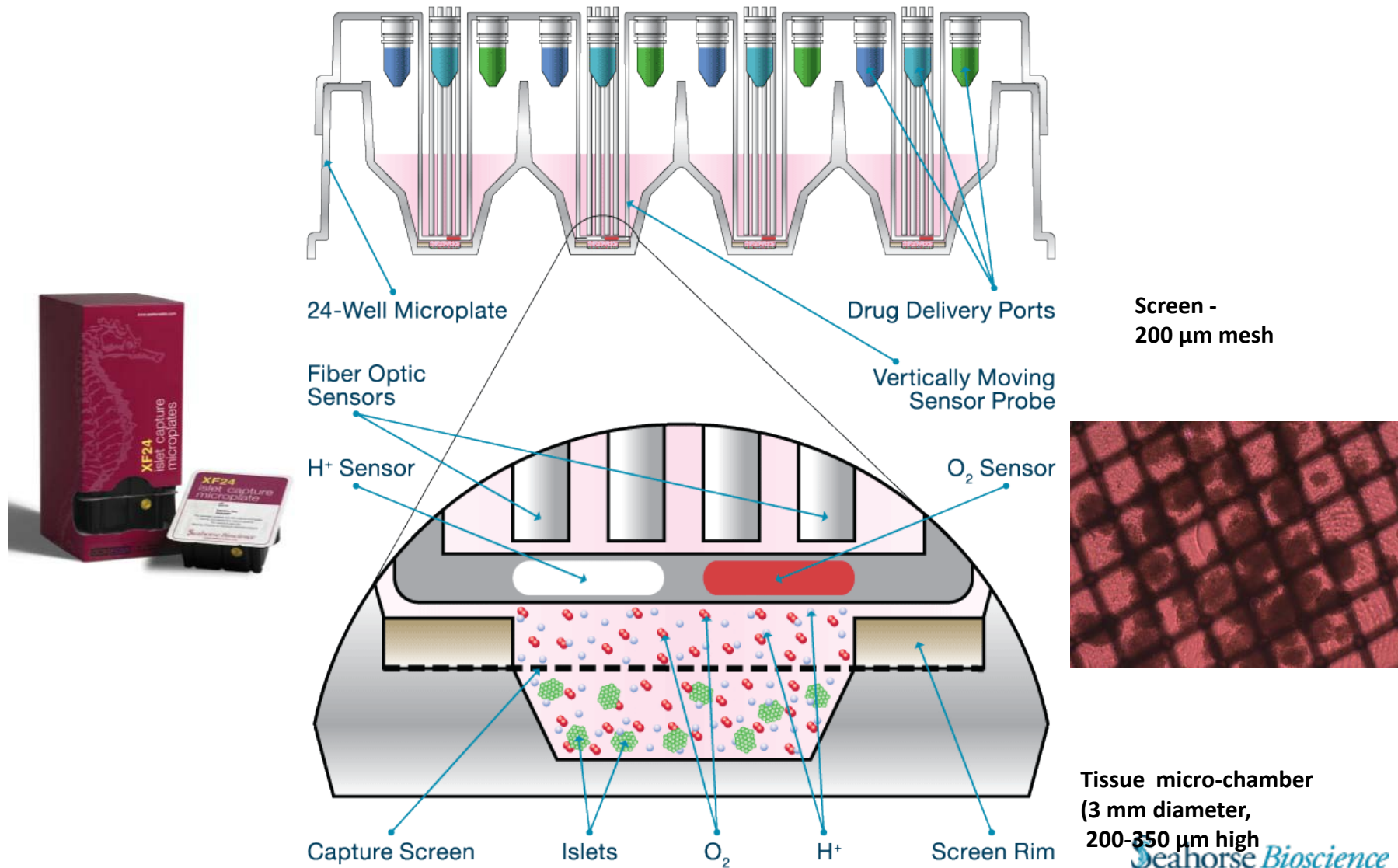
Anal. Biochem. (2010) Sept 1; 404(1):75-81

A high-throughput respirometric assay for mitochondrial biogenesis and toxicity

C.C. Beeson *et al.*

检测整体胰岛功能的胰岛捕获微孔板

Cutaway of a Probe & Islet Capture Well

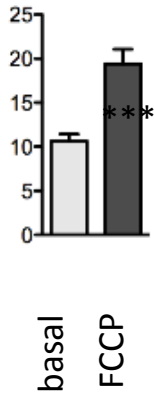
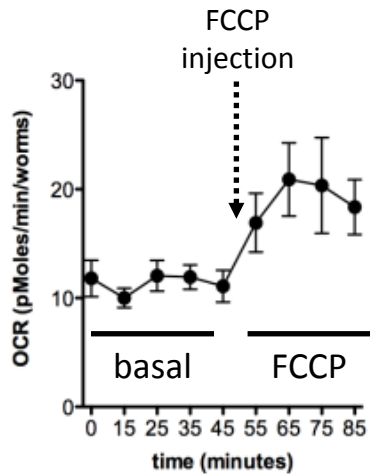


For research use only

*Figure not drawn to scale

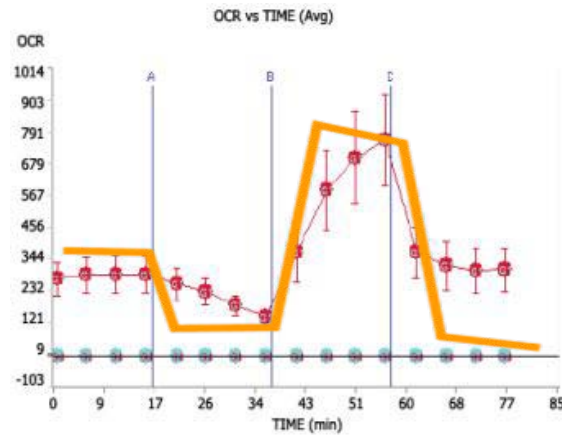
MODEL ORGANISMS

Beyond Cells



C.elegans

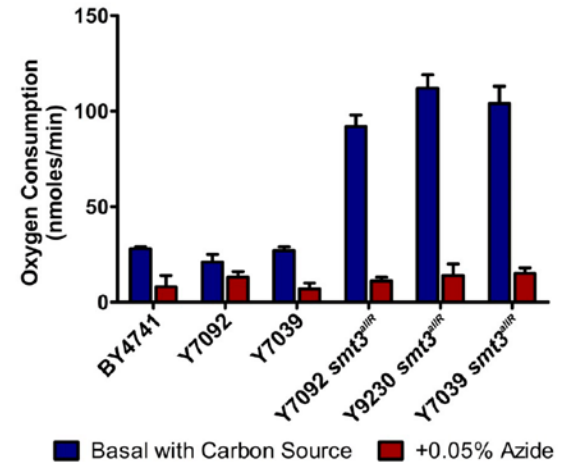
Data courtesy of Auwerx Lab
École Polytechnique Fédérale de Lausanne



Zebrafish

Bioenergetic profiling of zebrafish embryonic development

Stackley KD, Beeson CC, Rahn JJ, Chan SS.
PLoS One. 2011 6(9):e25652



Yeast

Global analysis of SUMO chain function reveals multiple roles in chromatin regulation

Tharan Srikumar, Megan C. Lewicki, Michael Costanzo, Johnny M. Tkach, Harm van Bakel, Kyle Tsui, Erica S. Johnson, Grant W. Brown, Brenda J. Andrews, Charles Boone, Guri Giaever, Corey Nislow, Brian Raught. J. Cell Biol. Vol. 201 No. 1 145-163