

THE IMMUNITY-METABOLISM LINK

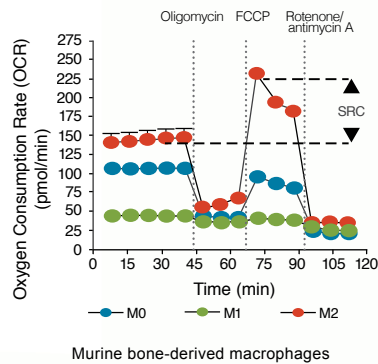
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**Cell Metabolism Assays  
for  
Immunology  
Research**

# GOLD STANDARD ASSAYS FOR MEASURING METABOLIC REPROGRAMMING

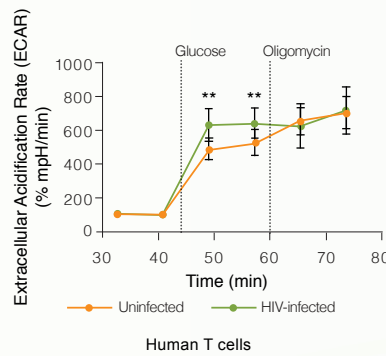
## METABOLIC SIGNATURES

Cell activation, amplification, and effector function are crucial aspects of the immune cell life cycle. Researchers are using XF technology to examine the cross-talk between immune cells and their metabolic signatures to gain insight into disease pathology, etiology, and possible treatment options. The XF Cell Mito Stress Test measures the key parameters of mitochondrial function: basal respiration, ATP-linked respiration, proton leak, maximal respiration, and spare respiratory capacity. The XF Glycolysis Stress Test measures the three key parameters of glycolytic function: glycolysis, glycolytic capacity, and glycolytic reserve.



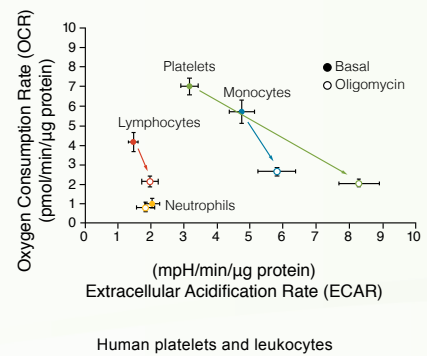
Huang SC *et al.*, (2014) Nat Immunol.

**XF Cell Mito Stress Test profiles metabolic signatures of activated bone marrow-derived macrophage subtypes.**



Hegedus A *et al.*, (2014) Retrovirology

**XF Assay reveals the role of glycolysis in HIV infection.**

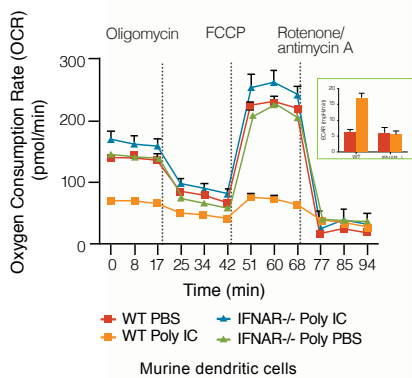


Kramer PA *et al.*, (2014) Redox Biol.

**XF Metabolic Switch Assay reveals distinct metabolic signatures in platelets and leukocytes.**

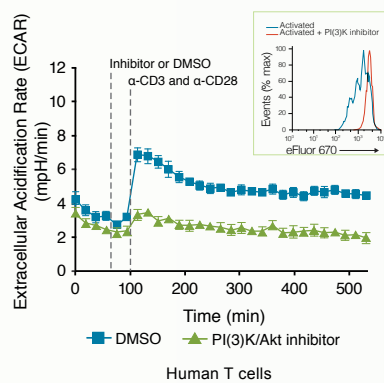
## METABOLIC REPROGRAMMING

Signaling plays an important role in eliciting immunological response by coordinating immune cell communication and actions. Researchers are using XF technology to probe the signaling and metabolic programming of immune cells.



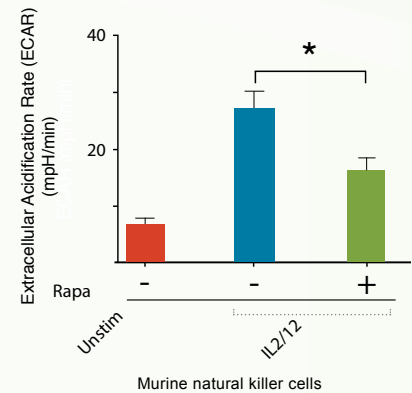
Pantel A *et al.*, (2014) PLoS Biol.

**XF Cell Mito Stress Test identifies IFNAR requirement for metabolic reprogramming.**



Gubser PM *et al.*, (2013) Nat Immunol.

**Real-time activation of memory T cells demonstrates a connection amongst signaling pathways, glycolysis, and proliferation.**



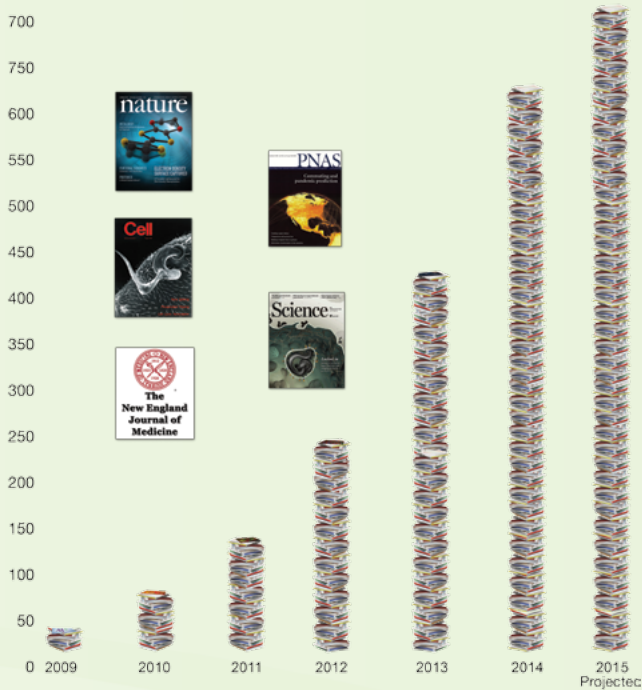
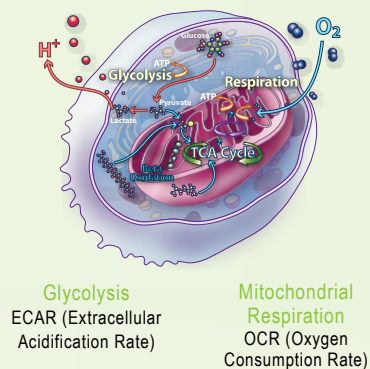
Donnelly RP *et al.*, (2014) J Immunol.

**XF Assay reveals Natural Killer (NK) cell dependence on mTORC1 following stimulation of IL-2 and IL-12.**

# THE WORLD'S MOST ADVANCED METABOLIC ANALYZERS

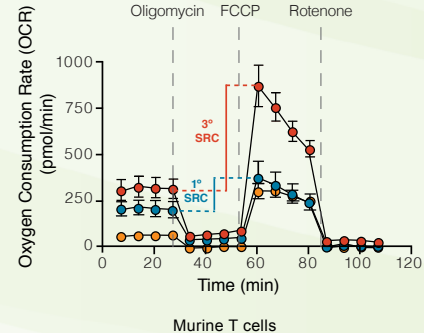
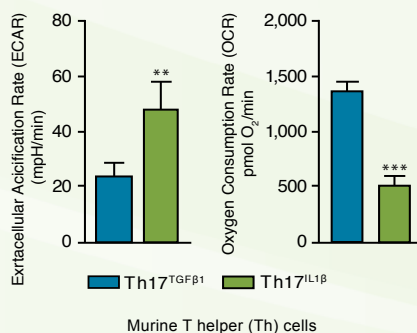
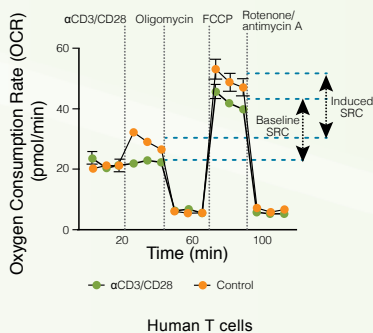
## PROVEN TECHNOLOGY FOR CUTTING EDGE RESEARCH

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 purposes.



## METABOLIC EFFECT OF THERAPEUTICS

The primary role of the immune system is to protect the host by targeting foreign antigens, controlling or clearing infections, and attacking cancerous cells. However, metabolic interventions present a largely untapped area of disease research. XF technology provides the necessary tools to understand the effects of therapeutic candidates on the antigen of interest, and on the immune system.



**Real-time activation reveals metabolic signatures of lupus patient-derived CD4<sup>+</sup> T cells.**

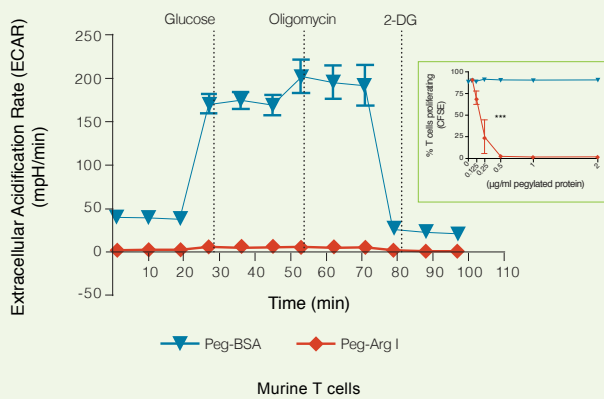
**XF Assays reveal a metabolic switch which correlates to the antitumor ability of Th17<sup>IL1β</sup> cells.**

**XF Assays reveal that tertiary immunization increases memory CD8<sup>+</sup> T cell recall.**

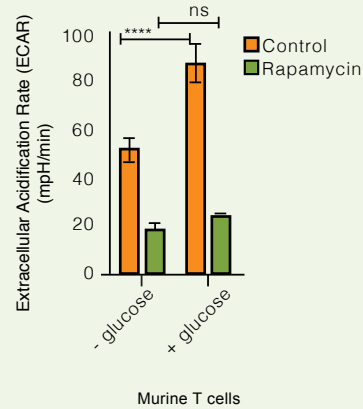
# MEASURING THE KEY PARAMETERS OF IMMUNOMETABOLISM

## SUBSTRATE UTILIZATION, FLEXIBILITY & DEPENDENCY

Each immune cell type has a specific function within the immune system. Cell fate decisions, activation, amplification, and effector function are driven by metabolism. To maintain the energy demands of the cell at each stage of its life cycle, the metabolic requirements for substrates or fuels that feed into the metabolic 'engines' are altered. XF technology provides the capability to examine the effect of substrate utilization and dependency, yielding powerful metabolic data.

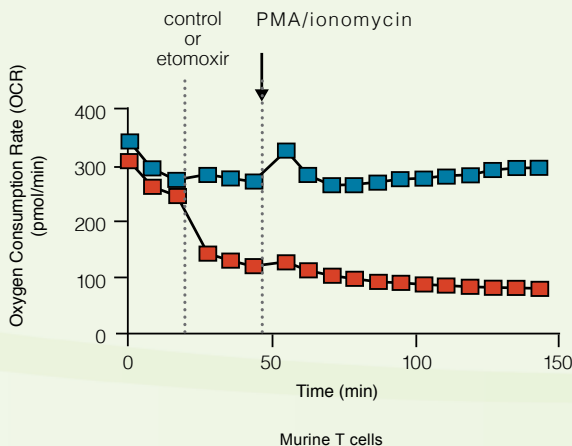


Murine T cells  
Fletcher M *et al.*, (2015) Cancer Res.



Murine T cells  
Goldberg EL, *et al.*, (2014) J Immol.

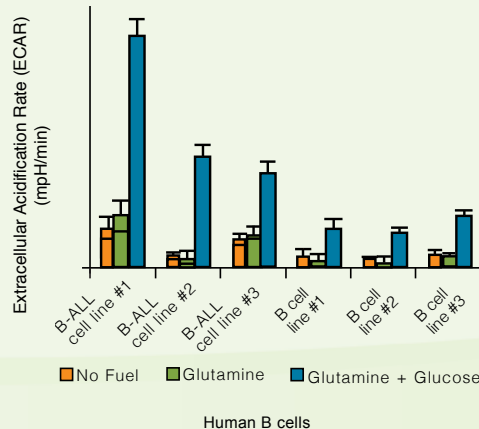
**XF Glycolysis Stress Test identifies L-Arginine dependence for proliferation in T cells.**



Murine T cells  
van der Windt GJ *et al.*, (2013) PNAS

**XF Assay reveals a role of fatty acid oxidation in memory T cell response.**

**XF Assay reveals glucose-insensitivity of naïve T cells in the presence of rapamycin.**



Human B cells  
Liu T *et al.*, (2014) Cell Death Dis.

**XF Assay reveals a glucose dependence in B-cell acute lymphoblastic leukemia (B-ALL) cells.**

# FUNCTIONAL XF METABOLIC ASSAYS - THE INTERSECTION OF IMMUNOLOGY & METABOLISM

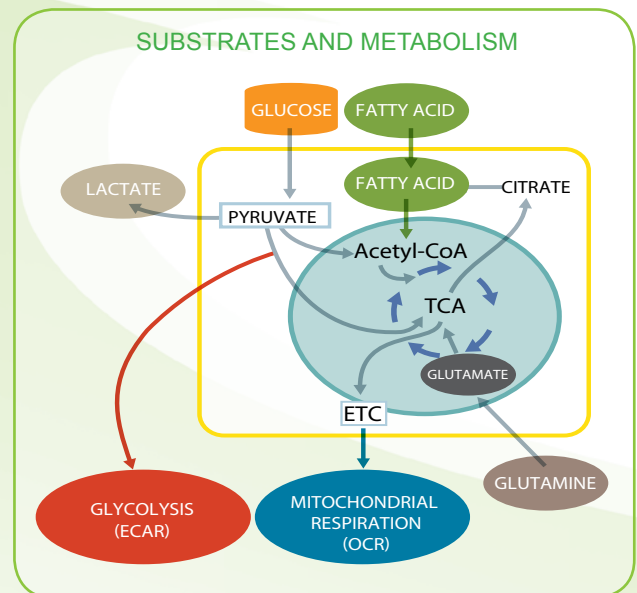
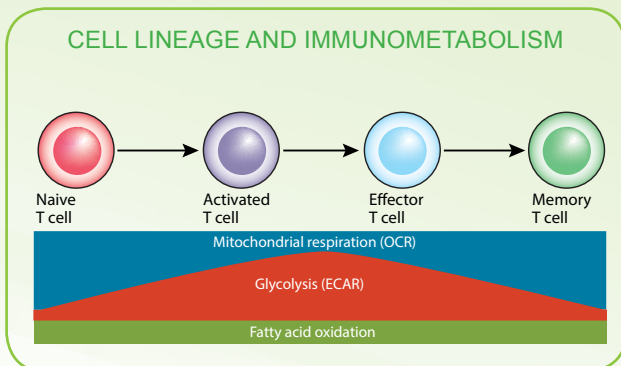
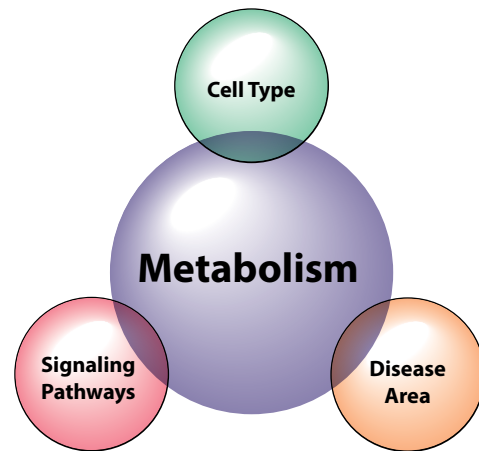
## XF TECHNOLOGY PROVIDES THE TOOLS TO MEASURE IMMUNOMETABOLISM

Immunologists study how the innate and adaptive immune system recognizes and responds to insults. Whether the research focus is on a specific immune cell type, signaling pathway, or disease area, immunologists are actively exploring the mechanisms that drive and perpetuate antigen recognition and response.

Immune system metabolism (referred to as 'immunometabolism') has emerged as a key mechanism in understanding the connection between metabolic pathways and immune responses. Each immune cell type has a specialized role in an immune response, as well as a preferred metabolic pathway to generate energy required to maintain homeostasis.

Research into metabolic changes provides insight into metabolic signature, signaling, and substrate preference. These metabolic choices are leading to new opportunities to modulate immunological response for therapeutic intervention.

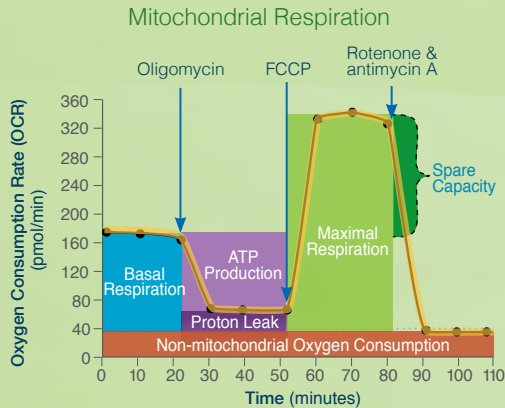
XF technology is at the forefront, providing powerful and effective tools to explore the burgeoning field of immunometabolism.



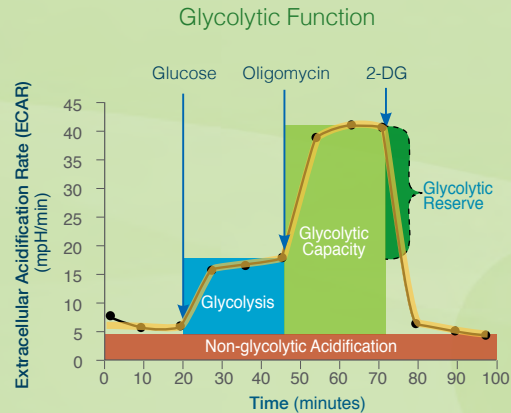
# GOLD STANDARD METABOLIC ASSAYS

MEASURING THE KEY PARAMETERS OF CELL METABOLISM

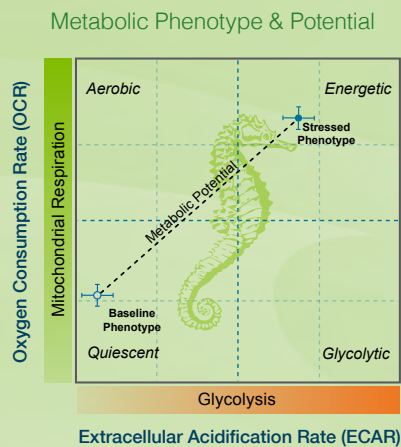
## XF Cell Mito Stress Test Profile



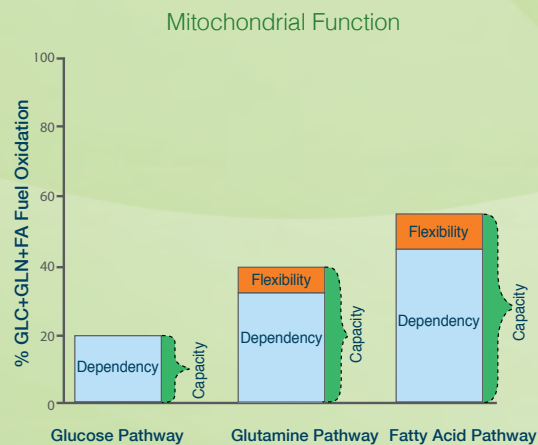
## XF Glycolysis Stress Test Profile



## XF Cell Energy Phenotype Test



## XF Mito Fuel Flex Test Profile



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