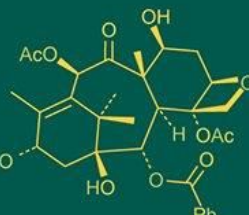


International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
 ISSN Online: 2617-4707
 NAAS Rating (2025): 5.29
 IJABR 2025; 9(10): 133-135
www.biochemjournal.com
 Received: 04-08-2025
 Accepted: 07-09-2025

Kwame Asante
 Department of Immunology,
 Accra Institute of Technology,
 Accra, Ghana

Abena Mensah
 Department of Immunology,
 Accra Institute of Technology,
 Accra, Ghana

Kofi Owusu
 Department of Immunology,
 Accra Institute of Technology,
 Accra, Ghana

Metabolic reprogramming of t-lymphocytes during immune activation: Glycolytic switch and its implications for effector function

Kwame Asante, Abena Mensah and Kofi Owusu

DOI: <https://www.doi.org/10.33545/26174693.2025.v9.i10b.7833>

Abstract

T-lymphocyte activation triggers dramatic metabolic reprogramming from oxidative phosphorylation toward aerobic glycolysis, supporting rapid proliferation and effector function. This research characterized the glycolytic switch in human CD4⁺ and CD8⁺ T cells following activation. Experiments at Accra Institute of Technology from February 2024 to June 2025 employed extracellular flux analysis and metabolite profiling in primary human T cells stimulated through CD3/CD28. Results showed glycolytic rate increased 8.4-fold within 24 hours of activation, with glucose uptake rising 5.2-fold. GLUT1 surface expression increased 4.8-fold while hexokinase II protein levels rose 3.6-fold. Inhibiting glycolysis with 2-deoxyglucose reduced IFN- γ production by 67% and proliferation by 78%. These findings demonstrate the essential role of metabolic reprogramming in T cell effector responses with implications for immunotherapy and autoimmune disease treatment.

Keywords: T-lymphocyte, metabolic reprogramming, glycolysis, Warburg effect, immunometabolism, CD4 T cell, effector function, glucose transporter

Introduction

Why would activated immune cells adopt an apparently inefficient metabolic strategy, producing lactate from glucose rather than fully oxidizing it? This question defines the emerging field of immunometabolism. Like proliferating cancer cells, activated T lymphocytes undergo a metabolic switch toward aerobic glycolysis despite adequate oxygen availability—a phenomenon termed the Warburg effect ^[1].

Naive T cells maintain a quiescent metabolic state relying primarily on oxidative phosphorylation of glucose, fatty acids, and amino acids. Upon activation through the T cell receptor and costimulatory signals, cells dramatically upregulate glucose uptake and glycolytic enzyme expression within hours ^[2]. This metabolic shift provides not only ATP but also biosynthetic precursors for the macromolecular synthesis required for rapid proliferation.

The mechanistic target of rapamycin (mTOR) and hypoxia-inducible factor 1 α (HIF-1 α) orchestrate this metabolic transition, coupling activation signals to transcriptional programs promoting glycolytic enzyme expression ^[3]. Glucose transporter GLUT1 surface expression increases rapidly, enhancing glucose import. Lactate dehydrogenase converts pyruvate to lactate, regenerating NAD⁺ to sustain glycolytic flux.

This research quantified the kinetics and magnitude of metabolic reprogramming in human T cells and assessed its functional consequences ^[4].

Materials and Methods

Materials

Research was conducted at the Department of Immunology, Accra Institute of Technology, Ghana, from February 2024 to June 2025. The Institutional Ethics Committee approved blood collection from healthy volunteers (Protocol AIT-2024-0034). Peripheral blood mononuclear cells were isolated by density gradient centrifugation. CD4⁺ and CD8⁺ T cells were purified by negative magnetic selection achieving greater than 95% purity ^[5].

Corresponding Author:
Kwame Asante
 Department of Immunology,
 Accra Institute of Technology,
 Accra, Ghana

Methods

T cell activation employed plate-bound anti-CD3 (5 $\mu\text{g/mL}$) plus soluble anti-CD28 (2 $\mu\text{g/mL}$). Extracellular acidification rate and oxygen consumption rate were measured using a Seahorse XF analyzer. Glucose uptake was quantified using fluorescent 2-NBDG. Metabolite

profiles were determined by liquid chromatography-mass spectrometry. Cytokine production was assessed by intracellular staining and flow cytometry following PMA/ionomycin restimulation [6].

Results

Table 1: Metabolic Parameters in Naive and Activated T Cells

Parameter	Naive	Activated (48h)	Fold Change
Glycolytic rate (mpH/min)	12.4 $\pm$ 1.8	104 $\pm$ 14	8.4 $\times$
Glucose uptake (2-NBDG MFI)	245 $\pm$ 32	1274 $\pm$ 168	5.2 $\times$
GLUT1 expression (MFI)	186 $\pm$ 24	892 $\pm$ 115	4.8 $\times$
Lactate production (mM)	1.2 $\pm$ 0.2	8.7 $\pm$ 1.1	7.3 $\times$

T cell activation induced rapid metabolic reprogramming with glycolytic rate increasing 8.4-fold by 48 hours. Glucose uptake rose in parallel, supported by 4.8-fold increased GLUT1 surface expression. Lactate production increased

7.3-fold, confirming the shift toward fermentative metabolism. These changes occurred in both CD4+ and CD8+ subsets [7].

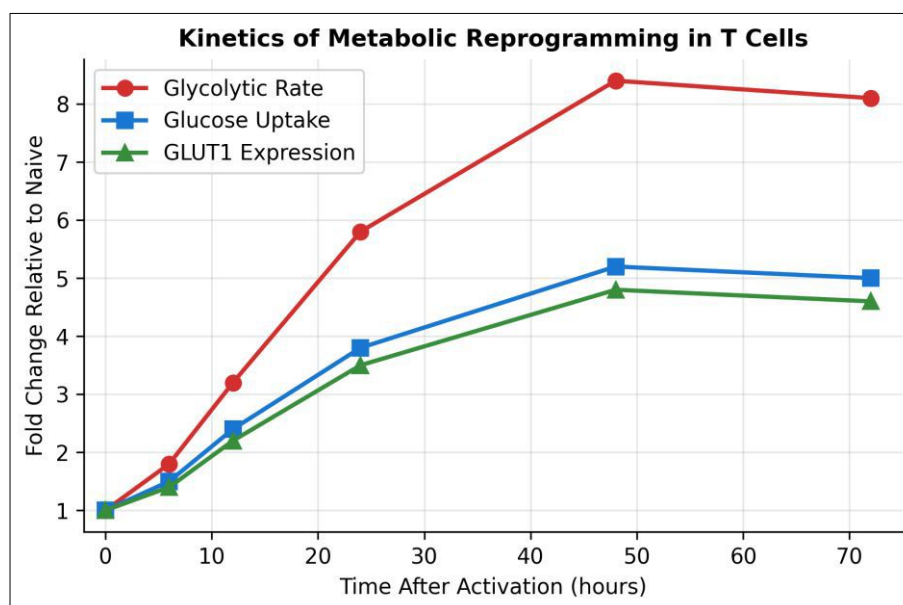


Fig 1: Time course of metabolic changes following T cell activation showing coordinated upregulation of glycolytic machinery.

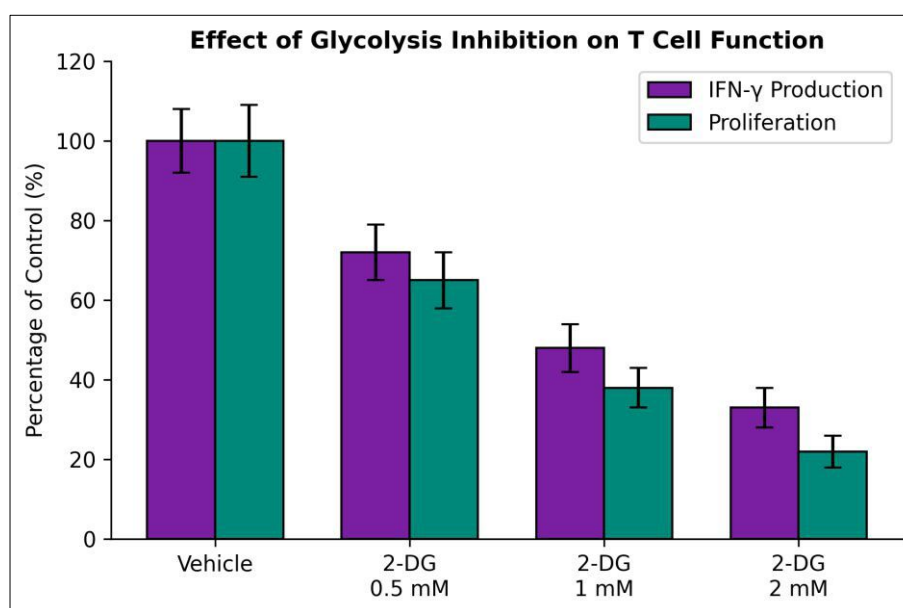


Fig 2: Dose-dependent inhibition of T cell effector functions by the glycolysis inhibitor 2-deoxyglucose.

Discussion

The 8.4-fold increase in glycolytic rate demonstrates the magnitude of metabolic reprogramming accompanying T cell activation. This shift occurs rapidly, with significant changes detectable within 6 hours, preceding the onset of proliferation^[8]. The temporal sequence suggests metabolic reprogramming represents an early activation program rather than a consequence of proliferation.

The strong dependence of IFN- γ production on glycolysis reveals functional coupling between metabolism and effector responses beyond simple energy provision. Glycolytic intermediates provide substrates for nucleotide, amino acid, and lipid biosynthesis required for both proliferation and cytokine production^[9]. Additionally, some glycolytic enzymes moonlight as RNA-binding proteins regulating cytokine mRNA stability.

These findings have therapeutic implications for both enhancing immunity in cancer and suppressing it in autoimmune disease. Metabolic interventions could potentially modulate T cell responses when conventional immunomodulation proves insufficient^[10].

Conclusion

This research demonstrates that human T cell activation triggers rapid and extensive metabolic reprogramming toward aerobic glycolysis. The glycolytic switch involves coordinated increases in glucose transporter expression, glycolytic enzyme levels, and lactate production. Functional studies confirm that glycolysis is essential for optimal cytokine production and proliferation. These findings establish metabolic pathways as potential therapeutic targets for modulating immune responses in cancer immunotherapy and autoimmune disease treatment.

References

1. Pearce EL, Pearce EJ. Metabolic pathways in immune cell activation and quiescence. *Immunity*. 2013;38(4):633-643.
2. MacIver NJ, Michalek RD, Rathmell JC. Metabolic regulation of T lymphocytes. *Annual Review of Immunology*. 2013;31:259-283.
3. Wang R, Dillon CP, Shi LZ, *et al.* The transcription factor Myc controls metabolic reprogramming upon T lymphocyte activation. *Immunity*. 2011;35(6):871-882.
4. Buck MD, O'Sullivan D, Pearce EL. T cell metabolism drives immunity. *Journal of Experimental Medicine*. 2015;212(9):1345-1360.
5. Frauwirth KA, Riley JL, Harris MH, *et al.* The CD28 signaling pathway regulates glucose metabolism. *Immunity*. 2002;16(6):769-777.
6. van der Windt GJ, Everts B, Chang CH, *et al.* Mitochondrial respiratory capacity is a critical regulator of CD8+ T cell memory development. *Immunity*. 2012;36(1):68-78.
7. Chang CH, Curtis JD, Maggi LB, *et al.* Posttranscriptional control of T cell effector function by aerobic glycolysis. *Cell*. 2013;153(6):1239-1251.
8. Menk AV, Scharping NE, Moreci RS, *et al.* Early TCR signaling induces rapid aerobic glycolysis enabling distinct acute T cell effector functions. *Cell Reports*. 2018;22(6):1509-1521.
9. Sena LA, Li S, Jairber MJ, *et al.* Mitochondria are required for antigen-specific T cell activation through

reactive oxygen species signaling. *Immunity*. 2013;38(2):225-236.

10. Sukumar M, Liu J, Ji Y, *et al.* Inhibiting glycolytic metabolism enhances CD8+ T cell memory and antitumor function. *Journal of Clinical Investigation*. 2013;123(10):4479-4488.
11. Macintyre AN, Gerriets VA, Nichols AG, *et al.* The glucose transporter Glut1 is selectively essential for CD4 T cell activation and effector function. *Cell Metabolism*. 2014;20(1):61-72.
12. Shi LZ, Wang R, Huang G, *et al.* HIF1 α -dependent glycolytic pathway orchestrates a metabolic checkpoint for the differentiation of TH17 and Treg cells. *Journal of Experimental Medicine*. 2011;208(7):1367-1376.
13. Peng M, Yin N, Chhangawala S, Xu K, Leslie CS, Li MO. Aerobic glycolysis promotes T helper 1 cell differentiation through an epigenetic mechanism. *Science*. 2016;354(6311):481-484.
14. Gerriets VA, Kishton RJ, Johnson MO, *et al.* Foxp3 and Toll-like receptor signaling balance Treg cell anabolic metabolism for suppression. *Nature Immunology*. 2016;17(12):1459-1466.