

In the format provided by the authors and unedited.

Ketogenesis activates metabolically protective $\gamma\delta$ T cells in visceral adipose tissue

Emily L. Goldberg^{1,2}, Irina Shchukina³, Jennifer L. Asher¹, Sviatoslav Sidorov¹, Maxim N. Artyomov³ ³ and Vishwa Deep Dixit^{1,2*}

¹Department of Comparative Medicine, Yale School of Medicine, New Haven, CT, USA. ²Department of Immunobiology, Yale School of Medicine, New Haven, CT, USA. ³Department of Pathology and Immunology, Washington University School of Medicine, St Louis, MO, USA. *e-mail: Vishwa.Dixit@yale.edu

Up-regulated Pathways

Pathway	Leading Edge Genes
NABA CORE MATRISOME	<i>Abi3bp, Spon2, Npnt, Matn2, Postn, Ddx26b, Nid1, Fmod, Pcolce, Igfbp4, Creld2, Aebp1, Igfbp6, Sparc, Lamc1, Gas6, Col1a1, Col5a2, Mfge8, Fbn1, Bgn, Efemp1, Col18a1, Mfap5, Col3a1, Emilin1, Igfbp7, Edil3, Eln, Col4a1, Cyr61, Col1a2, Col6a2, Fbln5, Fbln2, Col6a1, Col5a1, Ogn, Vwa9, Lrg1, Col4a2, Ctgf, Tinagl1, Igfbp3, Vwf, Prelp, Ltbp4, Fn1, Pxdn, Smoc2, Mmrn2, Spock2</i>
KEGG ECM RECEPTOR INTERACTION	<i>Itgb1, Itgb4, Cd47, Sdc1, Lamc1, Col1a1, Col5a2, Cd36, Itga5, Itga4, Col3a1, Cd44, Col4a1, Col1a2, Col6a2, Itga3, Itgb3, Col6a1, Col5a1, Col4a2, Itgb5</i>
REACTOME SEMAPHORIN INTERACTIONS	<i>Nrp1, Itgb1, Erbb2, Cdc42, Crmp1, Rac1, Semaph6a, Myl12b, Semaph4d, Dpysl3, Hsp90ab1</i>
PID A6B1 A6B4 INTEGRIN PATHWAY	<i>Itgb1, Erbb2, Itgb4, Ywhah, Rac1, Cd9, Lamc1, Ywhae, Pmp22</i>
REACTOME EXTRACELLULAR MATRIX ORGANIZATION	<i>Mmp25, Timp2, Pcolce, Serpinh1, Col1a1, Col5a2, Furin, Col3a1, Mmp17, Col4a1, Plod1, Ppib, P4hb, Col1a2, Col6a2, Col6a1, Col5a1, Col4a2</i>

Down-regulated Pathways

Pathway	Leading Edge Genes
PID IL12 2PATHWAY	<i>Atf2, Cd3g, Il2, Ccl4, Il18r1, Jak2, Il12rb1, Nfkb2, Il18rap, Ccr5, Ifng, Socs1, Il2rb, Relb, Il2ra, Tbx21, Stat1, Gadd45g, Il12rb2, Gadd45b</i>
REACTOME GROWTH HORMONE RECEPTOR SIGNALING	<i>Mapk3, Stat5a, Irs2, Jak2, Socs1, Cish, Sh2b1, Socs2, Stat1, Socs3</i>
REACTOME INTERFERON GAMMA SIGNALING	<i>Camk2d, Irf1, Oas3, Jak2, Ifng, Gbp4, Socs1, Icam1, Gbp2, Ifngr1, Gbp6, Irf8, Stat1, Ifngr2, Socs3</i>
REACTOME SRP DEPENDENT COTRANSLATIONAL PROTEIN TARGETING TO MEMBRANE	<i>Rps27a, Rps12, Rpl3, Srprb, Rpl17, Rpl23, Rpl29, Rpl26, Rpl27a, Rpl39, Rps14, Rpsa, Rpl13a, Rps9, Rpl27, Rps15a, Rplp2, Rpl41, Rpl35a, Rpl18, Rps23, Uba52, Rpl23a, Rpl18a, Rps28, Rpl36a, Fau, Rpl34, Rps16, Rps6, Rps21, Rpl13, Rps15, Rpl37, Rps7, Rps10, Rps5, Rps29, Rpl14, Rpl8, Rps24, Rps20, Rplp1, Rpl32, Rpl31, Rpl21, Rpl38, Rpl35, Rps27, Rpl37a, Rps18, Rpl36, Rps19, Rpl12, Rps25</i>
KEGG CYTOKINE CYTOKINE RECEPTOR INTERACTION	<i>Cxcl2, Il18r1, Tgfbr2, Il12rb1, Ccr8, Il18rap, Egfr, Ccr5, Ifng, Xcl1, Bmp7, Tnfrsf1b, Acvr2a, Il2rb, Tnfrsf1a, Vegfa, Il21r, Il10rb, Cxcl10, Tnf, Cxcr3, Ifnar2, Il2ra, Ifngr1, Il12rb2, Tnfrsf11, Ifngr2, Tnfrsf18, Lif</i>

Supplementary Table 1. GSEA gene lists of sorted adipose tissue $\gamma\delta$ T cells from 1 week KD vs Chow.

Leading edge genes for each pathway identified by Gene Set Enrichment Analysis. Up- and down- regulation indicates the direction of expression induced by KD as compared to Chow.

	% of calories			g/100 g diet		
	Carbohydrate	Protein	Fat	Carbohydrate	Protein	Fat
Control chow (3.1 kcal/g)	58	24	18	44.2	18.6	6.2
Ketogenic diet (6.76 kcal/g)	0.1	10.4	89.5	0.9	17.6	67.2

Supplementary Table 2. Diet compositions

Table containing the macronutrient composition of chow and KD diets based on percent of calories coming from each nutrient and percent of each nutrient by weight.