Supplemental Table 2. Gene Set Enrichment Analysis of Th1 and Th17 Cells Treated with GLS-Inhibitor

Th1 Cells: Increased Pathways with CB839 Treatment

Gene Set Name	# Genes in Gene Set (K)	Description	# Genes in Overlap (k)	k/K	p-value	FDR q-value
HALLMARK_E2F_TARGETS	200	Genes encoding cell cycle related targets of E2F transcription factors.	135	0.675	7.54E-170	3.77E-168
HALLMARK_G2M_CHECKPOINT	200	Genes involved in the G2/M checkpoint, as in progression through the cell division cycle.	101	0.505	3.74E-108	9.36E-107
HALLMARK_MITOTIC_SPINDLE	200	Genes important for mitotic spindle assembly.	56	0.28	4.54E-43	7.57E-42
HALLMARK_MTORC1_SIGNALING	200	Genes up-regulated through activation of mTORC1 complex.	47	0.235	1.53E-32	1.92E-31
HALLMARK_MYC_TARGETS_V1	200	A subgroup of genes regulated by MYC - version 1 (v1).	43	0.215	3.55E-28	3.55E-27
HALLMARK_IL2_STAT5_SIGNALING	200	Genes up-regulated by STAT5 in response to IL2 stimulation.	37	0.185	5.01E-22	4.18E-21
HALLMARK_GLYCOLYSIS	200	Genes encoding proteins involved in glycolysis and gluconeogenesis.	34	0.17	3.81E-19	2.72E-18
HALLMARK_DNA_REPAIR	150	Genes involved in DNA repair.	28	0.1867	4.05E-17	2.53E-16
HALLMARK_ESTROGEN_RESPONSE_LATE	200	Genes defining late response to estrogen.	30	0.15	1.60E-15	8.01E-15
HALLMARK_P53_PATHWAY	200	Genes involved in p53 pathways and networks.	30	0.15	1.60E-15	8.01E-15

Th1 Cells: Decreased Pathways with CB839 Treatment

Gene Set Name	# Genes in Gene Set (K)	Description	# Genes in Overlap (k)	k/K	p-value	FDR q-value
HALLMARK_KRAS_SIGNALING_UP	200	Genes up-regulated by KRAS activation.	20	0.1	6.52E-10	3.26E-08
HALLMARK_COMPLEMENT	200	Genes encoding components of the complement system, which is part of the innate immune system.	18	0.09	2.43E-08	4.05E-07
HALLMARK_INFLAMMATORY_RESPONSE	200	Genes defining inflammatory response.	18	0.09	2.43E-08	4.05E-07
HALLMARK_ALLOGRAFT_REJECTION	200	Genes up-regulated during transplant rejection.	17	0.085	1.36E-07	1.70E-06
HALLMARK_APICAL_JUNCTION	200	Genes encoding components of apical junction complex.	16	0.08	7.14E-07	7.14E-06
HALLMARK_APOPTOSIS	161	Genes mediating programmed cell death (apoptosis) by activation of caspases.	13	0.0807	6.99E-06	5.82E-05
HALLMARK_INTERFERON_GAMMA_RESPONSE	200	Genes up-regulated in response to IFNG [GeneID=3458].	14	0.07	1.61E-05	1.15E-04
HALLMARK_ANGIOGENESIS	36	Genes up-regulated during formation of blood vessels (angiogenesis).	6	0.1667	3.86E-05	2.41E-04
HALLMARK_UV_RESPONSE_DN	144	Genes down-regulated in response to ultraviolet (UV) radiation.	11	0.0764	5.83E-05	2.65E-04
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	200	Genes defining epithelial-mesenchymal transition, as in wound healing, fibrosis and metastasis.	13	0.065	6.88E-05	2.65E-04
HALLMARK_ESTROGEN_RESPONSE_EARLY	200	Genes defining early response to estrogen.	13	0.065	6.88E-05	2.65E-04

Th17 Cells: Increased Pathways with CB839 Treatment

Gene Set Name	# Genes in Gene Set (K)	Description	# Genes in Overlap (k)	k/K	p-value	FDR q-value
HALLMARK_INTERFERON_GAMMA_RESPONSE	200	Genes up-regulated in response to IFNG [GeneID=3458].	25	0.125	2.94E-13	1.47E-11
HALLMARK_APICAL_JUNCTION	200	Genes encoding components of apical junction complex.	19	0.095	2.09E-08	3.48E-07
HALLMARK_P53_PATHWAY	200	Genes involved in p53 pathways and networks.	19	0.095	2.09E-08	3.48E-07
HALLMARK_MYOGENESIS	200	Genes involved in development of skeletal muscle (myogenesis).	18	0.09	1.12E-07	1.40E-06
HALLMARK_COMPLEMENT	200	Genes encoding components of the complement system, which is part of the innate immune system.	17	0.085	5.62E-07	4.01E-06
HALLMARK_TNFA_SIGNALING_VIA_NFKB	200	Genes regulated by NF-kB in response to TNF [GeneID=7124].	17	0.085	5.62E-07	4.01E-06
HALLMARK_XENOBIOTIC_METABOLISM	200	Genes encoding proteins involved in processing of drugs and other xenobiotics.	17	0.085	5.62E-07	4.01E-06
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	200	Genes defining epithelial-mesenchymal transition, as in wound healing, fibrosis and metastasis.	16	0.08	2.66E-06	1.48E-05
HALLMARK_INFLAMMATORY_RESPONSE	200	Genes defining inflammatory response.	16	0.08	2.66E-06	1.48E-05
HALLMARK_HYPOXIA	200	Genes up-regulated in response to low oxygen levels (hypoxia).	15	0.075	1.18E-05	5.90E-05

Th17 Cells: Decreased Pathways with CB839 Treatment

Gene Set Name	# Genes in Gene Set (K)	Description	# Genes in Overlap (k)	k/K	p-value	FDR q-value
HALLMARK_E2F_TARGETS	200	Genes encoding cell cycle related targets of E2F transcription factors.	107	0.535	6.77E-130	3.38E-128
HALLMARK_G2M_CHECKPOINT	200	Genes involved in the G2/M checkpoint, as in progression through the cell division cycle.	94	0.47	7.15E-107	1.79E-105
HALLMARK_MYC_TARGETS_V1	200	A subgroup of genes regulated by MYC - version 1 (v1).	75	0.375	4.76E-76	7.94E-75
HALLMARK_MTORC1_SIGNALING	200	Genes up-regulated through activation of mTORC1 complex.	70	0.35	1.64E-68	2.05E-67
HALLMARK_MYC_TARGETS_V2	58	A subgroup of genes regulated by MYC - version 2 (v2).	31	0.5345	3.73E-38	3.73E-37
HALLMARK_IL2_STAT5_SIGNALING	200	Genes up-regulated by STAT5 in response to IL2 stimulation.	39	0.195	7.99E-28	6.66E-27
HALLMARK_CHOLESTEROL_HOMEOSTASIS	74	Genes involved in cholesterol homeostasis.	25	0.3378	8.83E-25	6.31E-24
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	113	Genes up-regulated during unfolded protein response, a cellular stress response related to the endoplasmic reticulum.	29	0.2566	1.17E-24	7.29E-24
HALLMARK_TNFA_SIGNALING_VIA_NFKB	200	Genes regulated by NF-kB in response to TNF [GeneID=7124].	34	0.17	2.14E-22	1.19E-21
HALLMARK_GLYCOLYSIS	200	Genes encoding proteins involved in glycolysis and gluconeogenesis.	31	0.155	2.53E-19	1.26E-18