

Figure legend:

Supplemental Figure 1. Purity of donor and host monocytes from patient PB collected 2 years post-BMT and purified using FACS sorting. A) Gating strategy for donor and host monocytes before sorting, A1, CD14+monocyte selection; A2. singlet selection; A3. Separation of donor and host monocyte based on donor HLA-specific Ab. B) Purity of isolated donor monocytes. B1. CD14+monocytes; B2. Singlet selection; B3. purity of isolated donor monocytes after sorting. C) Purity of isolated host monocytes. C1. CD14+monocytes; C2. Singlet selection. C3. purity of host monocytes after sorting.

Supplemental Table 1. Patient chimerism post-BMT (% donor)

Supplemental Table 2. Reconstitution of immune components post-BMT prior to and during thymopoiesis (cell numbers/ μ L by research FC).

Supplemental Table 3. Potential outcomes and mechanistic interpretation of Tolerance in different MLR set ups

Supplemental Table 4. Clinical chronology and graft characteristics

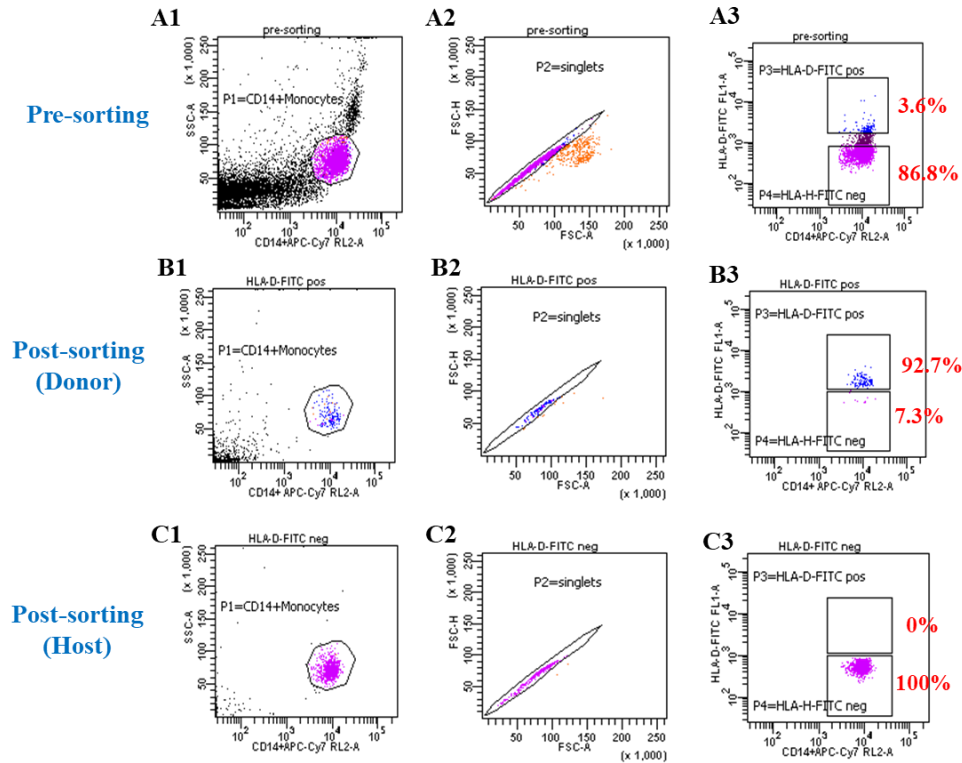
Supplemental Table 5. List of genes and their ranks in the downregulated ‘Allograft Rejection’ pathway analyzed by GSEA software, contrasting tolerant T cells (Tol T) and graft T cells (gT)¹ after *in vitro* stimulation with hDC.

Supplemental Table 6. Signaling pathway profile analyzed by GSEA software comparing tolerant T cells (2 years post-BMT) and graft T cells after *in vitro* stimulation with hDCs.

Supplemental Table 7. Signaling pathway profiles analyzed by IPA software contrasting circulating donor-derived tolerant T cells (Tol T, 2 years post-BMT) and donor bone marrow graft T cells (gT) after *in vitro* stimulation with hDCs.

Supplemental Table 8. Signaling pathway profiles analyzed by IPA software contrasting tolerant T cells (Tol T, 2 years post-BMT) and bone marrow graft T cells (gT) without any *in vitro* stimulation.

Supplemental Table 9. Signaling pathway profiles analyzed by IPA software contrasting co-existing circulating host and donor monocytes at 2 years post-BMT.



Supplemental Figure 1. Purity of donor and host monocytes from patient PB collected 2 years post-BMT and purified using FACS sorting. A) Gating strategy for donor and host monocytes before sorting, A1, CD14+monocyte selection; A2. singlet selection; A3. Separation of donor and host monocyte based on donor HLA-specific Ab. B) Purity of isolated donor monocytes. B1. CD14+monocytes; B2. Singlet selection; B3. purity of isolated donor monocytes after sorting. C) Purity of isolated host monocytes. C1. CD14+monocytes; C2. Singlet selection. C3. purity of host monocytes after sorting.

Supplemental Table 1. Patient chimerism post-BMT (% donor)

Chimerism	Post-BOLT/ pre-BMT	1m Post- BMT	2m	3m	6m	9m	1yr	1yr6m	2yrs	3yrs	4yrs	5yrs	6yrs	7yrs6m	9yrs6m
STR¹															
PB	0	100	72	52	24	21	26	30	28	22	23	17	22	20	21
CD3+T cells	N/A	N/A	27	N/A	94	93	100	95	97	93	92	89	96	96	96
CD33+ Myeloid cells	N/A	100	71	46	17	15	16	14	12	9	9	8	9	8	7
CD19+ B cells											69	62	28	39	38
FC² PB															
CD3+T cells	N/A	N/A	8.6	99.2	99.3	99.8	99.8	99.8	99.8	96.6	95.4	98.9	99.8	99.5	99.9
Monocyte (Myeloid)	N/A	N/A	58	40	22	19	17.2	13.5	10.6	13.1	13	7.2	11.3	7.2	6.3
NK cells	N/A	N/A	98	93	58	21	17	14	4.2	6	3.6	3.3	7.3	4	2.2
CD19+ B cells	N/A	N/A	N/A	N/A	N/A	95	94.3	91	86.8	69	81.4	78.7	66.7	61.6	42.6
FC² BAL															
CD3+T cells	N/A	N/A	N/A	N/A	99.4	99.4	99.2	97.2	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Monocyte (Myeloid)	N/A	N/A	N/A	N/A	42	34.5	24	24	N/A	N/A	N/A	N/A	N/A	N/A	N/A
NK cells	N/A	N/A	N/A	N/A	93	93	40	36	N/A	N/A	N/A	N/A	N/A	N/A	N/A
CD19+ B cells	N/A	N/A	N/A	N/A	N/A	N/A	63	46	N/A	N/A	N/A	N/A	N/A	N/A	N/A

¹**Short Tandem Repeat (STR)** testing in the clinical UPMC HLA-laboratory performed on MiniMACS™ purified populations. (There was only 1 test that could be conducted for each assay, and no SD was displayed).

²**Flow Cytometry (FC)** in research laboratory. (There was only 1 test that could be conducted for each assay, and no SD was displayed).

Supplemental Table 2. Reconstitution of immune components post-BMT prior to and during thymopoiesis (cell numbers/ μ L by research FC)

Immune components	Baseline	Post-BLOT/ pre-BMT	1m	2m	3m	6m	9m	1yr	1yr6m	2yrs	3yrs	4yrs	5yrs	6yrs	7yrs6m	9yrs6m
CD3+T cells	74	176	21	2.4	119	406	644	978	955	959	917	859	886	976	655	1334
CD4+T cells	30	25	16	2	98	361	541	753	716	676	628	574	634	646	430	912
CD4+FOXP3+Treg	N/A	2	N/A	N/A	1.5	5	1	6	4.4	22	4.7	8	N/A	25	N/A	N/A
CD4+Tcon¹	N/A	22	N/A	N/A	90	321	487	642	619	564	596	509	N/A	445	N/A	N/A
CD4+FOXP3+Treg/Tcon	N/A	0.08	N/A	N/A	0.02	0.02	0.002	0.01	0.01	0.04	0.01	0.02	N/A	0.06	N/A	N/A
CD4+T_{EM}²	N/A	11	N/A	N/A	16	81	129	192	234	129	82	194	62	N/A	N/A	N/A
CD4+T_{CM}³	N/A	14	N/A	N/A	80	250	306	390	152	256	255	188	251	N/A	N/A	N/A
CD4+Tnaive	N/A	0.4	0	0	2	25	88	159	269	276	277	237	222	233	168	374
CD8+T cells	24	98	2	0.4	19	39	86	187	203	249	236	237	213	280	194	386
CD8+T_{EM}⁴	N/A	46	N/A	N/A	7	7	5.4	28	19	14	12.5	29	21	N/A	N/A	N/A
CD8+T_{CM}⁵	N/A	28	N/A	N/A	11	5	11	35	3.4	14	16	5	25	N/A	N/A	N/A
$\gamma\delta$T cells	N/A	N/A	N/A	N/A	N/A	3	3	5	6	5	9	11	7	N/A	N/A	N/A
NK T cells	1	0.4	1.4	0	0.1	0.5	2	2	5	5	6.7	7.5	17	6.5	1.3	1.3
NK cells	227	308	173	149	92	208	159	373	215	240	211	173	291	268	211	417
CD19+ B cells	1	34	3	0.5	0.2	4	88	102	177	221	341	232	216	200	160	198
Monocytes	352	259	635	378	253	375	243	342	232	231	146	206	327	205	92	17.4
pDC⁶	6	24	35	7	6	11	7	4	13	7	11.6	8.8	10	9.7	9	7.7
mDC⁷	12	26	64	24	14	20	13	10	23	25	14.6	27	28.8	12	10	22
sjTREC⁸	N/A	369	0	0	0	677	1601	4486	1816	2085	N/A	N/A	N/A	N/A	N/A	N/A
TCRB SCS⁹	N/A	136	48	85	132	170	137	160	159	155	N/A	N/A	N/A	N/A	N/A	N/A

¹CD4+ Tcon = CD4+ conventional T cells (CD3+CD4+CD127+CD25+/-). ²CD4+ T_{EM}=CD4+ effector memory T cells (CD3+CD4+CD45RO+CD62L-).

³CD4+ T_{CM}=CD4+central memory T cells (CD3+CD4+CD45RO+CD62L+). ⁴CD8+ T_{EM}=CD8+effector memory T cells (CD3+CD8+CD45RO+CD62L-).

⁵CD8+ T_{CM}=CD8+central memory T cells (CD3+CD8+CD45RO+CD62L+). ⁶pDC=plasmacytoid dendritic cells. ⁷mDC=myeloid dendritic cells. ⁸sjTREC

value = copies/1E+05 T cells; ⁹TCRB SCS = TCR β spectratype complexity score, maximum SCS for 23 of V β tested = 184. (There was only 1 test that could be conducted for each assay, and no SD was displayed).

Supplemental Table 3. Potential outcomes and mechanistic interpretation of Tolerance in different MLR set ups.

Possible mechanisms	Clonal deletion	Suppression by Treg	Anergy	Suppression by Tr1
In vitro manipulation	—	IL-2 IT*	IL-2	Anti IL-10R Ab
Proliferation in MLR	--	↑	↑	↑
Cytokine Profiling in MLR Supe	--	↑ Th1, Th2, Th17	↑ Th1, Th2, Th17	↑IL-10
TCR Immunosequencing	Absent host-reactive clones	Representation of host-reactive clones	Representation of host-reactive clones	Representation of host-reactive clones

*IL-2-IT = IL-2-immunotoxin conjugate (Ontak™)

Supplemental Table 4. Clinical chronology and graft characteristics

Characteristics	Pt information
Disease	SCID (IL-7R)
Gender	Female
Age at BMT (years)	14
HLA-match (serological)	2/6
HLA-match (allele level)	1/8
Lung Tx date	9-25-2015
BMT date	1-28-2016
BMT CD34+ N°/kg	5E+06
BMT CD3+ N°/kg	8E+04
DLI date	4-5-2016
DLI CD3 N°/kg	5E+04
Stoppage date of FK506	5-5-2017
GvHD	Grade I, skin
Viral Infection	BKV

Supplemental Table 5. List of genes and their ranks in the downregulated ‘Allograft Rejection’ pathway analyzed by GSEA software contrasting tolerant T cells (Tol T) and graft T cells (gT)¹ after *in vitro* stimulation with hDC.

Row No.	SYMBOL	RANK IN GENE LIST ²	RANK METRIC SCORE ³	RUNNING ES ⁴	CORE ENRICHMENT ⁵
1	IL10	82	5.941	0.0213	No
2	CCL11	200	5.144	0.0308	No
3	TGFB2	482	3.756	0.0001	No
4	EGFR	714	3.286	-0.0239	No
5	FCGR2B	832	3.084	-0.0272	No
6	LY86	912	2.918	-0.0242	No
7	KRT1	954	2.843	-0.0144	No
8	CCL7	1079	2.659	-0.0217	No
9	CXCL13	1498	2.131	-0.0889	No
10	CCL13	1513	2.117	-0.0784	No
11	STAB1	1533	2.097	-0.069	No
12	TIMP1	1541	2.085	-0.0573	No
13	C2	1635	1.99	-0.0628	No
14	IL4R	1781	1.839	-0.0793	No
15	ICOSLG	2161	1.557	-0.1426	No
16	CTSS	2210	1.523	-0.1424	No
17	IFNGR1	2316	1.447	-0.1536	No
18	THY1	2436	1.378	-0.1679	No
19	CD79A	2578	1.288	-0.1871	No
20	ACVR2A	2704	1.212	-0.2036	No
21	CCL2	2737	1.191	-0.2023	No
22	FGR	2777	1.166	-0.2026	No
23	ITK	2840	1.136	-0.2074	No
24	MMP9	2900	1.1	-0.2119	No
25	SPI1	2905	1.098	-0.2058	No
26	CD7	3021	1.039	-0.2215	No
27	TLR3	3053	1.021	-0.2211	No
28	CCND2	3185	-1.036	-0.2399	No
29	IL15	3199	-1.044	-0.2359	No
30	LIF	3218	-1.05	-0.2328	No
31	GLMN	3221	-1.051	-0.2266	No
32	KLRD1	3303	-1.082	-0.2355	No
33	CD2	3360	-1.106	-0.2394	No
34	UBE2N	3364	-1.108	-0.233	No
35	SIT1	3456	-1.139	-0.2435	No
36	EIF5A	3468	-1.146	-0.2384	No
37	IL7	3593	-1.198	-0.2549	No
38	NPM1	3647	-1.227	-0.2574	No
39	MRPL3	3722	-1.258	-0.2638	No
40	MAP4K1	3802	-1.3	-0.271	No
41	P5MB10	3926	-1.38	-0.286	No
42	CD96	3984	-1.417	-0.2882	No
43	ST8SIA4	4051	-1.467	-0.2918	No
44	HLA-DQA1	4082	-1.488	-0.2882	No
45	TAP1	4137	-1.531	-0.2891	No
46	CD8A	4254	-1.63	-0.3013	Yes
47	IRF4	4263	-1.64	-0.2926	Yes
48	IL12RB1	4356	-1.731	-0.2995	Yes
49	IL18RAP	4394	-1.785	-0.2955	Yes
50	NME1	4412	-1.814	-0.2875	Yes
51	CD8B	4461	-1.891	-0.2849	Yes
52	DYRK3	4590	-2.048	-0.2968	Yes
53	CXCL9	4647	-2.132	-0.2943	Yes
54	ACHE	4745	-2.325	-0.2985	Yes
55	CCR5	4784	-2.402	-0.2908	Yes
56	BRCA1	4792	-2.418	-0.277	Yes
57	CCL5	4857	-2.534	-0.2736	Yes
58	FASLG	4860	-2.539	-0.2581	Yes
59	IL13	4918	-2.635	-0.2526	Yes
60	EREG	4919	-2.638	-0.2362	Yes
61	PRF1	4938	-2.689	-0.2229	Yes
62	IL4	4962	-2.743	-0.2102	Yes
63	IFNG	5025	-2.949	-0.2037	Yes
64	CXCR3	5045	-3.015	-0.1886	Yes
65	F2R	5091	-3.217	-0.1771	Yes
66	IL12A	5145	-3.621	-0.1648	Yes
67	CCR2	5163	-3.895	-0.1437	Yes
68	GZMB	5166	-3.953	-0.1194	Yes
69	GZMA	5211	-4.73	-0.0984	Yes
70	ELANE	5227	-5.321	-0.0681	Yes
71	PF4	5258	-11.829	0	Yes

¹The gT stimulated with hDC was used as a control in the comparison.

²Rank in gene list: gene rank in gene list based on their differential expression.

³Rank metric score: the value assigned to each gene in a ranked list, which determines its position within the list and is used to assess how significantly a gene is differentially expressed based on GSEA default metric (signal-to-noise ratio). The higher scores indicate genes that are more significantly differentially expressed (GSEA user guide).

⁴Running ES: Running enrichment score that is enrichment score at this point in the ranked list of genes.

⁵Core enrichment: genes with a ‘Yes’ value in this column contribute most to the enrichment result.

Supplemental Table 6. Signaling pathway profiles analyzed by GSEA software comparing tolerant T cells at (2 years post-BMT) and graft T cells after *in vitro* stimulation with hDCs.

2yrs Tol T+hDC vs gT+hDC (ctrl) Hallmark pathways	NES ¹	Nom p-value ²	FDR q-value ³	Size ⁴
<i>Downregulated (15/22 pathways)</i>				
G2M checkpoint	-4.82	0.00E+00	0.00E+00	116
E2F targets	-4.8	0.00E+00	0.00E+00	155
MYC targets v1	-4.23	0.00E+00	0.00E+00	102
Oxidative phosphorylation	-2.93	0.00E+00	0.00E+00	41
DNA repair	-2.81	0.00E+00	0.00E+00	38
MYC targets v2	-2.78	0.00E+00	0.00E+00	29
Mitotic spindle	-2.77	0.00E+00	0.00E+00	68
Spermatogenesis	-2.71	0.00E+00	0.00E+00	32
Heme metabolism	-2.31	0.00E+00	1.00E-03	63
mTORC1 signaling	-2.02	0.00E+00	3.00E-03	80
Allograft rejection	-1.99	0.00E+00	4.00E-03	71
IFN γ response	-1.53	6.00E-03	6.10E-02	60
Unfolded protein response	-1.52	3.30E-02	6.10E-02	32
IFN α response	-1.33	9.60E-02	1.57E-01	23
IL2/STAT5 signaling	-1.22	1.33E-01	2.48E-01	66
<i>Upregulated (7/22 pathways)</i>				
Epithelial mesenchymal transition	2.68	0.00E+00	0.00E+00	129
Myogenesis	1.83	1.13E-03	2.38E-02	72
UV response_DN	1.81	2.32E-03	2.18E-02	49
Apical junction	1.68	1.12E-03	4.80E-02	68
Estrogen response_early	1.68	1.00E-02	3.91E-02	72
Xenobiotic metabolism	1.56	3.16E-02	9.44E-02	47
Coagulation	1.46	5.04E-02	1.71E-01	57

¹**NES:** Normalized enrichment score which reflects the degree to which a gene set (or pathway) is concentrated at top (upregulated) or bottom (downregulated) of the ranked list of genes in the expression dataset. Higher NES value (positive or negative) suggests that the gene set is more likely to be associated with observed phenotype (GSEA user guide).

²**Nom p-value:** Nominal p-value represents statistical significance of a gene set's ES (GSEA user guide).

³**FDR q-value** is 'False discovery rate' that is the estimated probability that NES represents a false positive finding. GSEA recommends an FDR threshold of 0.25 or less. A lower q-value indicates a higher confidence in the significance of a gene set (GSEA user guide).

⁴**Size:** number of genes in the gene set after filtering out those genes not in the expression dataset (GSEA user guide).

Supplemental Table 7. Signaling pathway profiles analyzed by IPA software contrasting circulating donor-derived tolerant T cells (Tol T, 2 years post-BMT) and donor bone marrow graft T cells (gT) after *in vitro* stimulation.

2yrs Tol T+hDC vs gT+hDC (ctrl) ¹ Ingenuity Canonical Pathways	z-score ²	-log p-value ³	ratio ⁴
Pulmonary Fibrosis Idiopathic Signaling Pathway	6.328	5.3	0.311
Hepatic Fibrosis Signaling Pathway	5.176	2.3	0.258
Phagosome Formation	4.529	2.34	0.247
GP6 Signaling Pathway	4.352	1.4	0.274
Ferroptosis Signaling Pathway	4	2.11	0.299
Synaptogenesis Signaling Pathway	3.771	1.5	0.25
Colorectal Cancer Metastasis Signaling	3.677	1.49	0.254
Breast Cancer Regulation by Stathmin1	3.239	2.72	0.255
Wound Healing Signaling Pathway	3.222	6.11	0.34
Tumor Microenvironment Pathway	3.221	2.44	0.292
Pulmonary Healing Signaling Pathway	3.151	2.73	0.294
*CREB Signaling in Neurons	3.104	0.837	0.224
Bladder Cancer Signaling	3	3.66	0.351
Huntington's Disease Signaling	2.985	1.75	0.259
IL-15 Production	2.92	2.57	0.317
Regulation Of The Epithelial Mesenchymal Transition In Development Pathway	2.711	2	0.318
ID1 Signaling Pathway	2.517	2.41	0.286
ILK Signaling	2.496	3.85	0.318
Cardiac Hypertrophy Signaling (Enhanced)	2.449	1.53	0.24
Ephrin Receptor Signaling	2.263	2.96	0.299
GADD45 Signaling	2.236	1.93	0.339
Leukocyte Extravasation Signaling	2.16	1.37	0.259
Complement System	2	5.4	0.556
Ethanol Degradation IV	1.667	2.1	0.474
Chondroitin Sulfate Degradation (Metazoa)	1.633	1.31	0.429
Role of IL-17F in Allergic Inflammatory Airway Diseases	1.604	1.76	0.348
Cell Cycle: G1/S Checkpoint Regulation	1.528	3.33	0.388
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	1.46	6.74	0.54
Oxytocin In Spinal Neurons Signaling Pathway	-1.508	1.31	0.344
Salvage Pathways of Pyrimidine Ribonucleotides	-1.512	1.55	0.292
Urate Biosynthesis/Inosine 5'-phosphate Degradation	-1.633	1.87	0.5
Purine Nucleotides Degradation II (Aerobic)	-1.633	1.57	0.421
*Th1 Pathway	-1.789	0.442	0.222
Estrogen-mediated S-phase Entry	-1.886	7.91	0.731
FAT10 Signaling Pathway	-2	5.86	0.5
dTMP De Novo Biosynthesis	-2	2.13	0.8
Dilated Cardiomyopathy Signaling Pathway	-2.117	1.65	0.277
RAN Signaling	-2.121	1.89	0.471
RHO GDI Signaling	-2.412	4.3	0.321
Cyclins and Cell Cycle Regulation	-2.646	4.32	0.398
Purine Nucleotides De Novo Biosynthesis II	-2.646	2.64	0.636
Granzyme B Signaling	-2.646	2.08	0.5
Pyrimidine Deoxyribonucleotides De Novo Biosynthesis I	-2.714	2.51	0.478
BER (Base Excision Repair) Pathway	-3.441	3.25	0.432
Kinetochore Metaphase Signaling Pathway	-3.92	13.8	0.542
Cell Cycle Control of Chromosomal Replication	-5.24	11	0.625

¹Comparison was made of the activation status for signaling pathways between circulating T cells (donor origin) in tolerant state (Tol T) 2-years post-BMT and graft T cells (gT). Both cell types were stimulated with hDC *in vitro*, with graft T cells + hDC serving as a control. The comparison utilized RNAseq gene differential expression data sets generated by CLC Genomics Workbench software and well-established signaling pathways database from IPA software.

²**z-score:** IPA software calculates an 'activation z-score' for each pathway, indicating whether the pathway is likely to be activated or inhibited based on the direction of expression changes in the genes involved, as compared with the IPA database. Pathways were selected if their z-score ≥ 2 or ≤ -2 .

³**-log p-value:** It's a transformed version of p-value that interprets the significance of pathway. IPA uses a default threshold of -log p-value ≥ 1.3 . The higher value holds greater significance.

⁴**Ratio:** proportion of presented dataset genes in the total number of genes in that pathway within the IPA reference set.

*These 2 pathways had z-score ≥ 2 or ≤ -2 after hDC stimulation even though their -log p-value < 1.3 .

Supplemental Table 8. Signaling pathway profiles analyzed by IPA software contrasting tolerant T cells (Tol T, 2 years post-BMT) and bone marrow graft T cells (gT) without any *in vitro* stimulation.

2yrs Tol T vs g (ctrl) Ingenuity Canonical Pathways	z-score ²	-log p-value ³	Ratio ¹	2yrs Tol T vs g (ctrl) Ingenuity Canonical Pathways	z-score ²	-log p-value ³	Ratio ¹
RHO GDI Signaling	3.922	3.24	0.226	PKC α Signaling in T Lymphocytes	-3.138	1.52	0.178
PPAR Signaling	3.71	1.48	0.212	Osteoarthritis Pathway	-3.159	10.9	0.315
Antioxidant Action of Vitamin C	3.638	1.86	0.224	Putrescine Degradation III	-3.162	4.62	0.588
PTEN Signaling	2.858	3.37	0.247	Tryptophan Degradation X (Mammalian, via Tryptamine)	-3.162	4.06	0.526
CLEAR Signaling	2.335	1.94	0.192	Oxidative Ethanol Degradation III	-3.162	2.31	0.345
Extrinsic Prothrombin Activation Pathway	2.236	2.75	0.235	Oxytoxin In Spinal Neurons Signaling Pathway	-3.162	1.97	0.312
LXR/RXR Activation	1.976	4.15	0.276	Phospholipase	-3.207	1.96	0.285
IGF-1 Signaling	-1.508	1.48	0.212	Sphingosine-1-phosphate Signaling	-3.266	3.49	0.265
Apolin Adipocyte Signaling Pathway	-1.604	1.26	0.209	Thrombin Signaling	-3.266	1.97	0.2
T Cell Exhaustion Signaling Pathway	-1.606	1.5	0.178	Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	-3.286	1.45	0.191
Aryl Hydrocarbon Receptor Signaling	-1.789	3.55	0.252	Ethanol Degradation	-3.317	3.18	0.407
TLR Pathway	-1.8	7.11	0.323	Fc γ RIIIR Signaling in B Lymphocytes	-3.317	1.67	0.229
Gol Signaling	-1.8	3.02	0.243	Dermatan Sulfate Biosynthesis (Late Stages)	-3.317	1.54	0.262
eNOS Signaling	-1.826	2.66	0.23	Ephrin B Signaling	-3.357	2.34	0.264
Inhibition of Angiogenesis by TSP1	-1.89	3.04	0.375	Relaxin Signaling	-3.357	1.69	0.205
OX40 Signaling Pathway	-1.89	1.6	0.189	Ephrin Receptor Signaling	-3.411	3.52	0.243
Neuregulin Signaling	-1.941	2.3	0.235	STAT3 Pathway	-3.413	7.87	0.333
Savage Pathways of Pyrimidine Deoxyribonucleotides	-2	1.55	0.444	TEC Kinase Signaling	-3.443	5	0.224
Prostanoid Biosynthesis	-2	1.38	0.4	Ethanol Degradation IV	-3.464	5.91	0.632
Oleate Biosynthesis II (Animals)	-2	1.38	0.4	Noradrenaline and Adrenaline Degradation	-3.464	3.34	0.4
Pentose Phosphate Pathway	-2	1.38	0.4	Serotonin Degradation	-3.528	2.33	0.281
Corticotropin Releasing Hormone Signaling	-2.041	1.41	0.197	B Cell Receptor Signaling	-3.528	26.9	0.368
VDNR/RAR Activation	-2.111	0.247	0.01	CXCR4 Signaling	-3.53	2.79	0.229
Actin Nucleation by ARP-WASP Complex	-2.121	2.45	0.253	PLK Signaling in B Lymphocytes	-3.53	1.79	0.212
Regulation of Actin-based Motility by Rho	-2.138	2.91	0.255	MSP-RON Signaling in Cancer Cells Pathway	-3.53	1.28	0.194
Mitotic Roles of Polo-Like Kinase	-2.138	2.25	0.27	Sperm Motility	-3.545	8.57	0.287
Natural Killer Cell Signaling	-2.16	2.57	0.218	Dopamine Degradation	-3.606	5.31	0.542
Cytclins and Cell Cycle Regulation	-2.183	1.39	0.187	Actin Cytoskeleton Signaling	-3.651	0.229	0.277
Epithelial Adherens Junction Signaling	-2.197	2.51	0.226	Cell Cycle Control of Chromosomal Replication	-3.742	1.66	0.25
CD42 Signaling	-2.236	3.25	0.208	WNT/Ca ²⁺ pathway	-3.771	2.89	0.292
Remodeling of Epithelial Adherens Junctions	-2.236	2.81	0.288	Pancreatic Adenocarcinoma Signaling	-3.771	1.61	0.21
Ecicosanoid Signaling	-2.236	2.11	0.262	Leukocyte Extravasation Signaling	-3.795	4.2	0.249
Phenylalanine Degradation IV (Mammalian, via Side Chain)	-2.236	1.42	0.357	Gol Signaling	-3.8	1.61	0.21
GolT2/3 Signaling	-2.268	1.96	0.218	Systemic Lupus Erythematosus In T Cell Signaling	-3.812	1.65	0.178
Estrogen-mediated S Signaling	-2.333	2.14	0.346	Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	-3.9	5.06	0.281
IL-1 Signaling	-2.333	1.58	0.219	GNRH Signaling	-3.962	1.25	0.185
Antiproliferative Role of Somatostatin Receptor 2	-2.333	1.28	0.216	ERK5 Signaling	-4	1.86	0.243
Tryptophan Degradation to 2-amino-3-carboxymuconate Semialdehyde	-2.449	5.09	1	IKK Signaling	-4.004	2.73	0.221
Choline Biosynthesis III	-2.449	2.06	0.429	Regulation Of The Epithelial Mesenchymal Transition	-4.012	3.14	0.229
Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17F	-2.449	1.49	0.333	Growth Factors Pathway	-4.017	2.31	0.229
Regulation Of The Epithelial Mesenchymal Transition In Development Pathway	-2.524	2.17	0.247	Factors Promoting Cardiogenesis in Vertebrates	-4.017	2.31	0.229
Cardiac β -adrenergic Signaling	-2.524	2.08	0.221	Fc γ Receptor-mediated Phagocytosis in Macrophages and Monocytes	-4.025	1.46	0.215
ERK/MAPK Signaling	-2.556	2.6	0.214	Cholecystokinin/Gastrin-induced Signaling	-4.025	1.42	0.205
RHO Signaling	-2.6	1.95	0.221	HMGB1 Signaling	-4.041	3.78	0.252
TLR Pathway	-2.646	5.95	0.316	Systemic Lupus Erythematosus In B Cell Signaling Pathway	-4.093	3.1	0.36
Role of IL-17A in Psoriasis	-2.646	2.81	0.5	Xenobiotic Metabolism AHF Signaling Pathway	-4.146	2.57	0.266
Inflammasome pathway	-2.646	1.79	0.35	Endothelin-1 Signaling	-4.226	1.71	0.199
Role of NANOG in Mammalian Embryonic Stem Cell Pluripotency	-2.646	1.62	0.212	NF- κ B Signaling	-4.234	3.44	0.207
Noch Signaling	-2.646	1.53	0.227	Synaptogenesis Signaling Pathway	-4.243	1.45	0.179
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	-2.646	1.45	0.304	Gol Signaling	-4.263	3.02	0.25
RAC Signaling	-2.668	2.3	0.226	IDI Signaling Pathway	-4.45	6.31	0.276
PDGF Signaling	-2.668	1.26	0.209	TREM1 Signaling	-4.49	8.61	0.341
Paritins Signaling	-2.673	2.51	0.245	HIF1 α Signaling	-4.629	5.09	0.225
Toll-like Receptor Signaling	-2.673	2.91	0.247	Phospholipase C Signaling	-4.629	3.61	0.22
HGF Signaling	-2.683	4.3	0.275	Neurovascular Tissue Regeneration Pathway	-4.629	1.81	0.197
Nitric Oxide Signaling in the Cardiovascular System	-2.683	1.31	0.202	Adrenomedullin signaling pathway	-4.644	2.53	0.216
Macropinocytosis Signaling	-2.714	4.56	0.329	Globlastoma Multiforme Signaling	-4.667	4.9	0.268
NAD Biosynthesis II (from tryptophan)	-2.828	4.75	0.277	Integrin Signaling	-4.667	2.31	0.25
Fatty Acid α -oxidation	-2.828	3.15	0.5	Role of Hypercytokinemia/hyperchemokinein in the Pathogenesis of Influenza	-4.667	2.87	0.271
Role of IL-17F in Alcoholic Inflammatory Airway Diseases	-2.828	1.62	0.261	GTP Signaling Pathway	-4.707	2.7	0.242
Basal Cell Carcinoma Signaling	-2.84	2.12	0.257	White Adipose Tissue Browning Pathway	-4.707	1.56	0.204
Glioma Signaling	-2.84	1.46	0.205	IL-15 Production	-4.727	8.63	0.358
Gustation Pathway	-2.874	1.28	0.185	IL-17 Signaling	-4.727	3.97	0.212
IL-15 Signaling	-2.887	2.91	0.426	Cardiac Hypertrophy Signaling	-4.768	1.81	0.192
cAMP-mediated signaling	-2.887	4.23	0.238	Signaling by Rho Family GTPases	-4.841	5.03	0.242
Chondroitin Sulfate Biosynthesis (Late Stages)	-2.887	1.7	0.267	NAD Signaling	-4.914	1.28	0.193
Apolin Adipocyte Signaling Pathway	-2.982	1.67	0.207	Neuroinflammation Signaling Pathway	-4.993	5.67	0.241
Histamine Degradation	-3	5.02	0.692	Wound Healing Signaling Pathway	-5.345	4.15	0.235
Tryptophan Degradation III (Eukaryotic)	-3	3.18	0.407	IL-17 Signaling	-5.376	2.69	0.223
Gloma Invasiveness Pathway	-3	2.8	0.282	Xenobiotic Metabolism PXR Signaling Pathway	-5.667	1.86	0.205
PCP (Planar Cell Polarity) Pathway	-3	2.49	0.283	FAF Signaling	-5.762	7.55	0.321
Glycine-mediated Detoxification	-3	2.02	0.333	IL-8 Signaling	-6.112	5.44	0.262
14-3-3-mediated Signaling	-3	1.53	0.206	Pulmonary Healing Signaling Pathway	-6.147	6.85	0.284
Chemokine Signaling	-3	1.4	0.221	Colorectal Cancer Metastasis Signaling	-6.181	6.7	0.261
Ovarian Cancer Signaling	-3.051	2.46	0.224	Hepatic Fibrosis Signaling Pathway	-6.188	7.77	0.244
Dermatan Sulfate Biosynthesis	-3.051	1.39	0.246	G-Protein Coupled Receptor Signaling	-6.237	4.93	0.249
Pyroptosis Signaling Pathway	-3.128	2.52	0.256	Tumor Microenvironment Pathway	-6.472	4.91	0.264
Endocannabinoid Neuropathic Pain Pathway	-3.128	1.81	0.209	Dendritic Cell Maturation	-6.525	7.79	0.249
PAK Signaling	-3.13	4.24	0.282	Breast Cancer Regulation by Statmin1	-6.755	5.54	0.211
P2Y Purinergic Receptor Signaling Pathway	-3.13	1.76	0.211	Pulmonary Fibrosis Idiopathic Signaling Pathway	-7.18	6.34	0.245
Crosstalk between Dendritic Cells and Natural Killer Cells	-3.138	5.36	0.33	Cardiac Hypertrophy Signaling (Enhanced)	-7.298	6.61	0.223
Regulation of Macrophage Signaling Pathway	-3.138	5.09	0.333	CREB Signaling in Neurons	-8.171	6.01	0.213

¹Comparison was made of the activation status for signaling pathways between circulating T cells (donor origin) in tolerant state (Tol T) 2-years post-BMT and graft T cells (gT), without hDC *in vitro* stimulation. Graft T cells served as a control. The comparison utilized RNAseq gene differential expression data sets generated by CLC Genomics Workbench software and well-established signaling pathways database from IPA software.

²z-score: IPA software calculates an 'activation z-score' for each pathway, indicating whether the pathway is likely to be activated or inhibited based on the direction of expression changes in the genes involved, as compared with the IPA. Pathways were selected if their z-score ≥ 2 or ≤ -2 .

³-log p-value: It's a transformed version of p-value that interprets the significance of pathway. IPA uses a default threshold of -log p-value ≥ 1.3 . The higher value holds greater significance.

⁴**Ratio**: proportion of presented dataset genes in the total number of genes in that pathway within the IPA reference set.

Supplemental Table 9. Signaling pathway profiles analyzed by IPA software contrasting co-existing circulating host and donor monocytes at 2 years post-BMT.

2yrs hMono vs 2yrs dMono (ctrl) ¹ Ingenuity Canonical Pathways	z-score ²	-log p-value ³	Ratio ⁴	2yrs hMono vs 2yrs dMono (ctrl) ¹ Ingenuity Canonical Pathways	z-score ²	-log p-value ³	Ratio ⁴	2yrs hMono vs 2yrs dMono (ctrl) ¹ Ingenuity Canonical Pathways	z-score ²	-log p-value ³	Ratio ⁴
Neutrophil degranulation	11.415	39.7	0.54	The citric acid (TCA) cycle and respiratory electron transport	1.921	5.33	0.545	RAB GEFs exchange GTP for GDP on RABs	1.915	1.95	0.371
SRP-dependent cotranslational protein targeting to membrane	8.102	29.9	0.772	Aggri Interactions at Neuromuscular Junction	1.887	3.54	0.456	Caspase activation via Death Receptors in the presence of ligand	1.897	2.69	0.625
Eukaryotic Translation Initiation	7.398	25.3	0.713	Apelin Adipocyte Signaling Pathway	1.887	1.44	0.349	Valine Degradation I	1.897	2.31	0.55
Eukaryotic Translation Elongation	7.171	21.9	0.737	HMGB1 Signaling	1.885	4.73	0.409	TRAIL signaling	1.89	3.34	0.675
Schizosaccharomyces acid metabolism	7.14	19.6	0.602	TCR signaling	1.869	12.1	0.556	CSDE1 Signaling Pathway	1.877	2.94	0.455
Eukaryotic Translation Termination	7.034	20.5	0.723	RAS processing	1.84	3.82	0.625	TCF dependent signaling in response to WNT	1.812	4.75	0.392
Response of EIF2AK4 (GCN2) to amino acid deficiency	6.905	21.1	0.709	Mitophagy	1.84	2.45	0.5	Transcriptional Regulation by VENTX	1.807	1.83	0.425
Nonsense-Mediated Decay (NMD)	6.333	22.3	0.692	Signaling by CSF3 (G-CSF)	1.84	2.45	0.5	Intrinsic Pathway for Apoptosis	1.8	2.94	0.455
Oxidative Phosphorylation	5.899	18	0.664	MAPK targets/ Nuclear events mediated by MAP kinases	1.84	1.97	0.455	Angiopoietin Signaling	1.789	2.25	0.395
Microautophagy Signaling Pathway	5.612	7.48	0.459	MyD88-independent TLR4 cascade	1.837	4.24	0.568	RHOA Signaling	1.769	3.51	0.402
TP53 Regulates Metabolic Genes	5.461	9.88	0.58	Signaling by Insulin receptor	1.828	1.83	0.419	EPH1-Ephrin signaling	1.761	3.47	0.424
Cellular response to hypoxia	5.376	6.54	0.533	Fcy Receptor-mediated Phagocytosis in Macrophages and Monocytes	1.795	2.71	0.398	Cholecystokinin-Gastrin-mediated Signaling	1.761	2.54	0.376
Electron transport, ATP synthesis, and heat production by uncoupling proteins	5.237	20.7	0.656	Transcriptional regulation by RUNX1	1.794	4.51	0.408	Epithelial Adhesion Junction Signaling	1.756	8.31	0.471
Autophagy	5.222	5.38	0.397	Cargo recognition for clathrin-mediated endocytosis	1.777	3.06	0.4	Role of p14p19ARF in Tumor Suppression	1.732	1.33	0.414
Class I MHC mediated antigen processing and presentation	5.157	10.4	0.411	Signaling by the B Cell Receptor (BCR)	1.734	2.94	0.365	p53 Signaling	1.706	1.76	0.377
Interleukin-1 family signaling	5.077	6.21	0.457	Neuroinflammation Signaling Pathway	1.714	4.8	0.365	Oncostatin M Signaling	1.698	2.2	0.442
Cachexia Signaling Pathway	5.058	4.74	0.356	Glutathione Redox Reactions I	1.714	2.05	0.5	Apoptophagy	1.698	1.5	0.395
Major pathway of rRNA processing in the nucleolus and cytosol	5.051	14.6	0.527	CDP-diacylglycerol Biosynthesis I	1.714	1.58	0.444	Circadian Clock	1.698	1.31	0.362
Necroptosis	5.027	5.4	0.388	Chaperone Mediated Autophagy	1.673	3.71	0.636	Apelin Endothelial Signaling Pathway	1.677	3.1	0.381
Interleukin-10 signaling	4.95	9.67	0.711	Remodeling of Epithelial Adhesion Junctions	1.673	2.32	0.409	OAS antiviral response	1.633	1.94	0.667
Degradation of beta-catenin by the destruction complex	4.824	8.05	0.538	TRIM1 Signaling	1.667	5.1	0.5	Pathogenesis of Multiple Sclerosis	1.633	1.94	0.667
Mitotic Metaphase and Anaphase	4.796	5.45	0.391	Alpha protein kinase I signaling pathway	1.646	2.06	0.636	TNF signaling	1.616	5.45	0.544
Autophagosome Formation	4.796	5.24	0.605	Proteophagy	1.646	2.06	0.636	TBC/RABGAPs	1.606	2.07	0.432
Regulation of mitotic cell cycle	4.743	4.35	0.455	Amoid fiber formation	1.646	1.94	0.384	UVC-Induced MAPK Signaling	1.606	1.96	0.412
Mitochondrial protein import	4.585	4.6	0.5	RAF/MAP kinase cascade	1.626	5.3	0.382	PUK/ARF Signaling	1.605	4.84	0.394
Neutrophil Extracellular Trap Signaling Pathway	4.585	11.5	0.418	Role of MAPK Signaling in Inhibiting the Pathogenesis of Influenza	1.6	1.44	0.355	Transcriptional Regulation by NF- κ B	1.604	1.35	0.4
Macrophage Classical Activation Signaling Pathway	4.5	3.16	0.367	Protein folding	1.592	4.18	0.439	Translocation of SLCA24 (GLUT4) to the plasma membrane	1.569	1.57	0.366
Iron uptake and transport	4.491	2.2	0.414	Doubtfulquintation	1.574	5.75	0.388	RAC Signaling	1.54	5.91	0.445
Hedgehog ligand biogenesis	4.459	5.41	0.523	Folate Signaling Pathway	1.558	1.76	0.393	Seritol Cell-Germ Cell Junction Signaling Pathway (Enhanced)	1.539	6.54	0.408
Necroptosis Signaling Pathway	4.45	2.52	0.359	Regulation of Actin-based Motility by the	1.555	3.17	0.4	MicroRNA Biogenesis Signaling Pathway	1.522	4.79	0.399
KEAP1-NFE2L2 pathway	4.427	3.95	0.44	Glycerophospholipid biosynthesis	1.535	1.69	0.354	IL-17A Signaling in Gastric Cells	1.508	2.18	0.5
Regulation of Apoptosis	4.352	7.69	0.623	Superpathway of Cholesterol Biosynthesis	1.5	4.03	0.607	Dopamine Degradation	1.508	1.59	0.458
NIK--noncanonical NF- κ B signaling	4.352	5.91	0.55	Signaling by FGF23	1.5	1.48	0.4	Glycolysis I	1.508	1.59	0.458
CGAS-STING Signaling Pathway	4.341	2.99	0.381	Cholesterol biosynthesis	1.496	2.37	0.52	RIPK1-mediated regulated necrosis	1.5	2.58	0.5
Sphingolipid metabolism	4.243	1.85	0.368	Multiple Sclerosis Signaling Pathway	1.492	2.3	0.338	Wound Healing Signaling Pathway	1.463	2.26	0.332
Synthesis of DNA	4.23	3.2	0.395	Mitotic Prophase	1.48	5.05	0.456	Signaling by TGF-beta Receptor Complex	1.46	2.43	0.434
TNFR2 non-canonical NF- κ B pathway	4.218	6.95	0.559	Immunogenic Cell Death Signaling Pathway	1.475	2.1	0.381	MSP-RON Signaling in Macrophages (Enhanced)	1.474	3.19	0.397
Protein Sorting Signaling Pathway	4.007	5.08	0.407	COP1-mediated anterograde transport	1.469	3.47	0.416	Globulins Multifunction Signaling	1.511	3.34	0.375
COP1-mediated vesicle transport	4.004	3.78	0.458	Nucleotide Excision Repair	1.466	2.43	0.385	Breast Cancer Regulation by Statins	1.516	2.59	0.308
C-type lectin receptors (CLRs)	3.966	11.8	0.531	FAT10 Signaling Pathway	1.449	5.9	0.564	Lymphotxin β Receptor Signaling	1.528	2.68	0.444
RAB geranylgeranylation	3.9	3.16	0.446	Ephrin Receptor Signaling	1.449	3.06	0.358	NAD Signaling Pathway	1.543	1.57	0.331
Ceramide Signaling	3.893	5.15	0.473	Endocannabinoid Cancer Inhibition Pathway	1.449	3.05	0.377	HER-2 Signaling in Breast Cancer	1.565	6	0.404
Metabolism of polyamines	3.889	5.57	0.542	NLR signaling pathways	1.449	2.43	0.429	Ribonucleotide Reductase Signaling Pathway	1.576	2.49	0.353
DNA Replication Pre-Initiation	3.833	4.53	0.442	Pentose Phosphate Pathway	1.449	1.65	0.6	ATM Signaling	1.667	4.81	0.455
Hedgehog 'on' state	3.812	5.97	0.5	Signaling by FERB4	2.4	1.87	0.397	Interleukin-7 signaling	1.667	1.61	0.356
Response to elevated platelet cytosolic Ca ²⁺	3.81	4.05	0.409	Toll Like Receptor 3 (TLR3) Cascade	2.397	3.65	0.562	BBSome Signaling Pathway	1.69	2	0.304
Hepatic Cholestasis	3.787	1.44	0.313	Crosstalk between Dendritic Cells and Natural Killer Cells	2.353	1.79	0.363	ERYTHROPOIETIN Signaling Pathway	1.692	2.4	0.351
ISG15 antiviral mechanism	3.78	2.13	0.394	Signaling by NTRK1 (TRKA)	2.335	2.08	0.383	RUNX1 regulates megakaryocyte differentiation and platelet function	1.698	2.55	0.431
Detoxification of Reactive Oxygen Species	3.771	2.66	0.486	Advanced glycosylation endproduct receptor signaling	2.333	2.92	0.692	G alpha (12/13) signalling events	1.768	2.47	0.4
Pathogen Induced Cytokine Storm Signaling Pathway	3.714	3.54	0.341	Vitamin C Transport	2.333	1.32	0.435	Huntington's Disease Signaling	1.769	7.15	0.401
MyD88-MAL/TRAF6 cascade initiated on plasma membrane	3.71	3.22	0.5	IL-8 Signaling	2.321	3.89	0.374	Orexin Signaling Pathway	1.789	2.78	0.345
Peroxisomal protein import	3.674	1.7	0.381	Insertion of tail-anchored proteins into the endoplasmic reticulum membrane	2.309	2.44	0.545	Glyoxalase A Signaling	1.808	5.78	0.521
Regulation of RUNX2 expression and activity	3.667	4.93	0.493	TCA Cycle II (Eukaryotic)	2.309	2.44	0.545	Parkinson's Signaling Pathway	1.857	6.9	0.395
Signaling by NOTCH4	3.647	8.93	0.573	Phosphatidylcholine Biosynthesis II (Non-plastidic)	2.309	1.71	0.448	Formation of WDRE5-containing histone-modifying complexes	1.886	1.95	0.429
NAF1-D Signaling Pathway	3.622	4.55	0.382	Energy dependent regulation of mTOR by LKB1-AMPK	2.294	3.89	0.414	Signaling by SCF-KIT	1.886	1.83	0.419
Transcriptional regulation by RUNX3	3.507	6.12	0.49	TAK1-dependent IKK and NF- κ B activation	2.294	3.85	0.523	Pulmonary Fibrosis Idiopathic Signaling Pathway	1.91	2.07	0.317
Cargo concentration in the ER	3.5	2.24	0.471	Toll-like Receptor Signaling	2.294	3.49	0.442	Synaptogenesis Signaling Pathway	1.925	5.13	0.369
MHC class II antigen presentation	3.464	2.86	0.381	Sensence-Associated Secretory Phenotype (SASP)	2.268	1.94	0.384	ROBO SLIT Signaling Pathway	1.941	4.26	0.419
Mitochondrial translation	3.452	2.43	0.385	MAP kinase signaling	2.236	3.27	0.513	HIPPO Signaling	1.964	2.49	0.395
E3 ubiquitin ligases ubiquitinate target proteins	3.413	5.9	0.564	Role of PKR in Interferon Induction and Antiviral Response	2.188	3.45	0.394	Signaling by PDGF	1.964	1.31	0.362
RHO GTPases Activate WASP and WAVEs	3.411	5.13	0.611	Cholesterol Biosynthesis I	2.121	2.17	0.615	Integrin cell surface interactions	2.121	2.01	0.376
Protein ubiquitination	3.357	2.45	0.5	Cholesterol Biosynthesis II (via 24,25-dihydrocholesterol)	2.121	2.17	0.615	Spliceosomal Cycle	2.132	2.43	0.434
Fc epsilon receptor (FCER1) signaling	3.347	3.89	0.374	Gene Silencing by RNA	2.121	1.3	0.337	Small Cell Lung Cancer Signaling	2.132	1.58	0.351
ABC-family proteins mediated transport	3.328	7.62	0.515	Amino acids regulate mTORC1	2.117	3.81	0.491	Aldosterone Signaling in Epithelial Cells	2.335	3.09	0.369
PTEN Regulation	3.328	7.27	0.46	Interconversion of nucleotide di- and triphosphates	2.111	1.91	0.5	Netrin-1 signaling	2.4	2.07	0.42
MyD88 dependent cascade initiated on endosome	3.3	3.89	0.581	Ferroptosis Signaling Pathway	2.066	1.95	0.338	Sensory processing of sound by outer hair cells of the cochlea	2.4	1.56	0.382
Regulation of mRNA stability by proteins that bind AU-rich elements	3.3	1.72	0.409	Mitotic G2-M phases	2.063	10.4	0.472	ECF Signaling	2.4	1.47	0.375
Cell Cycle Checkpoints	3.266	3.61	0.353	Regulation of lipid metabolism by PPARalpha	2.058	1.31	0.328	CRFB Signaling in Neurons	2.514	2.12	0.301
Role of MAPK Signaling in Promoting the Pathogenesis of Influenza	3.244	2.33	0.373	TCF- β Signaling	2.043	1.39	0.34	Adrenergic Receptor Signaling Pathway (Enhanced)	2.54	1.59	0.321
EIF2 Signaling	3.204	25.2	0.595	Clathrin-mediated endocytosis	2.023	4.72	0.426	Sensory processing of sound by inner hair cells of the cochlea	2.6	1.47	0.362
S Phase	3.202	3.93	0.43	MTOR signaling	2	3.4	0.571	Glycan Assembly	2.65	8.51	0.446
NRF2 mediated Oxidative Stress Response	3.162	4	0.374	Chlorothione Redox Reactions II	2	2.36	1	NCAM signaling for neurite out growth	2.711	1.6	0.377
Cristae formation	3.153	3.3	0.548	Regulation of TP53 Expression and Degradation	2	1.59	0.41	Histone Modification Signaling Pathway	2.714	3.07	0.34
Endosomal Sorting Complex Required For Transport (ESCRT)	3.153	3.3	0.548	Zymosterol Biosynthesis	2	1.39	0.667	Neuropathic Pain Signaling in Dorsal Horn Neurons	2.744	1.41	0.34
NOD1/2 Signaling Pathway	3.098	2.32	0.347	DMPL Signaling in Neutrophils	1.98	7.47	0.481	GPS Signaling Pathway	2.744	1.46	0.333
Cytotecton by HMOX1	3.053	4.48	0.5	NBP(S) activates chaperone genes	1.964	2.31	0.438	RHO GTPase cycle	2.708	10.3	0.396
Actin Nucleation by DRP-WASP Complex	3.053	4.33	0.451	Induction of Apoptosis by HIV-1	1.961	2.66	0.429	Docosahexaenoic Acid (DHA) Signaling	3.313	7.56	0.438
MyD88 cascade initiated on plasma membrane	3.051	2.37	0.52	Cellular response to heat stress	1.961	2.08	0.371	Neutrin and neurotrophins	3.71	1.39	0.368
Mitotic G1 phase and G1/S transition	3	6.74	0.466	Th1 Pathway	1.953	8.6	0.513	Acetylcholine Receptor Signaling Pathway	3.81	1.73	0.325
Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17E	3	1.64	0.5	Chemosensory	1.941	2.37	0.52	Mitochondrial Dysfunction	4.11	14.7	0.456
Protein Ubiquitination Pathway	2.997	9.3	0.429	Thrombin signalling through protease-activated receptors (PARs)	1.941	1.34	0.406	Extracellular matrix organization	4.333	1.46	0.34
Acute Phase Response Signaling	2.994	14.1	0.391								
Late endosomal microautophagy	2.982	3.77	0.559								
Signaling by ROBO receptors	2.941	4.86	0.44								

¹A comparison of the activation status of signaling pathways between host-monocytes (hMono) and donor monocytes (dMono) at tolerant stage 2-years post-BMT. The dMono was used as a control in comparison. The comparison was based on their RNAseq gene differential expression data sets generated by CLC Genomic Workbench software and the database of well-established signaling pathways from IPA software.

²**z-score:** IPA software calculates an 'activation z-score' for each pathway, indicating whether the pathway is likely to be activated or inhibited based on the direction of expression changes in the genes involved, as compared with the IPA database. Pathways were selected if their z-score ≥ 2 or ≤ -2 .

³**-log p-value:** It's a transformed version of p-value that interprets the significance of pathway. IPA uses a default threshold of -log p-value ≥ 1.3 . The higher value holds greater significance.

⁴**Ratio:** proportion of presented dataset genes in the total number of genes in that pathway within the IPA reference set.