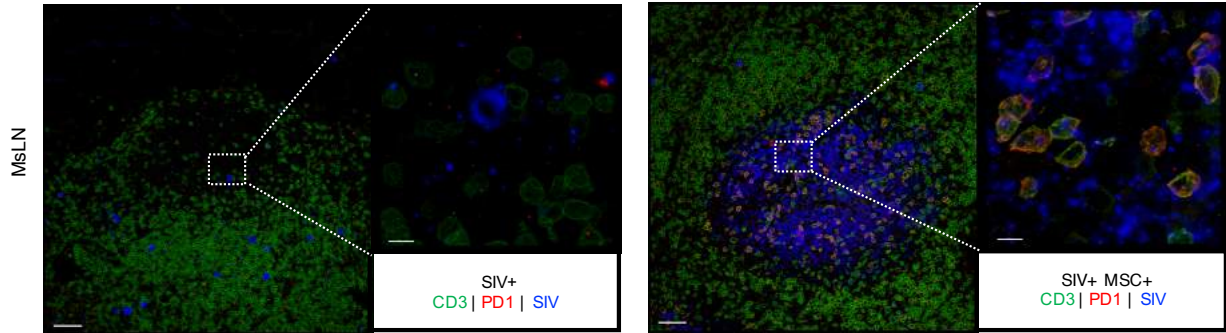
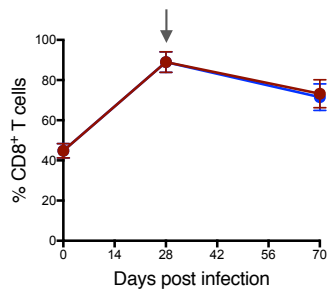


## SUPPLEMENTARY MATERIALS

**A**

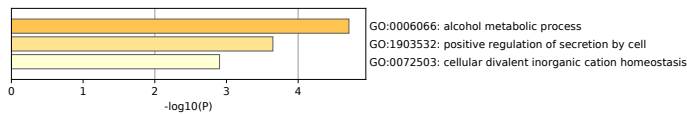


**B**

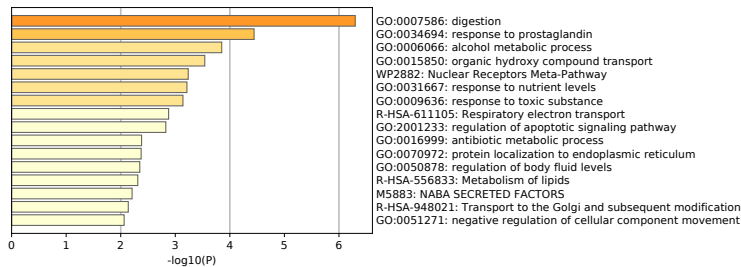


**Supplementary Figure 1. Detection of viral loads in the periphery and localization in the tissue. (A)** Dual in situ RNA hybridization and immunohistochemistry analysis of GC of the MsLN of SIV+MSC+ and SIV+, respectively, showing viral RNA (blue), T cells (green) and PD-1 (red). Magnification 20x and 100x. Scale bars 20 $\mu$ m and 50 $\mu$ m. **(B)** Longitudinal percentage of CD4<sup>+</sup> T cells in the gut (SIV+ n = 7 and SIV+MSC+ n = 5). Data represent the mean ( $\pm$  SEM) for each time point. Grey arrow represents the first MSC administration.

**A** DOWN: SIV+ vs. SIV-



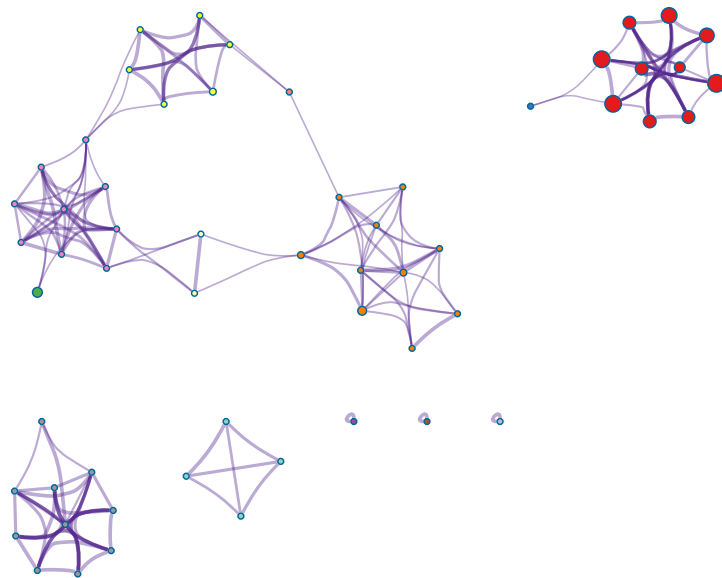
**B** DOWN: SIV+MSC+ vs. SIV-



**C** SIV+ vs. SIV-

Gene Count/ Enriched Pathway Key

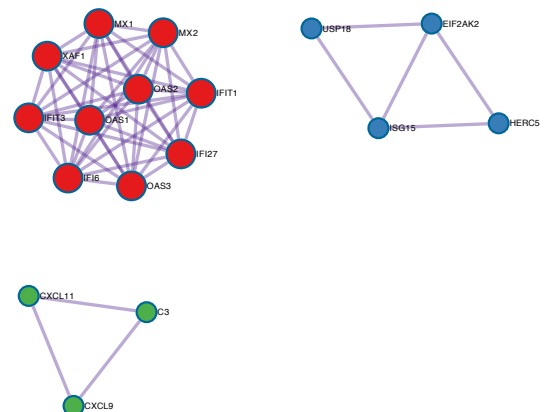
- 16 ■ Defense response to virus
- 5 ■ Type II interferon signaling (IFNG)
- 9 ■ Response to bacterium
- 3 ■ Response to interferon-alpha
- 4 ■ Regulation of defense response to virus
- 6 ■ Negative regulation of hydrolase activity
- 3 ■ Non-genomic actions of 1,25 dihydroxy vitamin D3
- 4 ■ Positive regulation of transmembrane transport
- 4 ■ Establishment of vesicle localization
- 4 ■ Regionalization
- 3 ■ Viral carcinogenesis
- 3 ■ Extrinsic apoptotic signaling pathway
- 4 ■ Regulation of inflammatory response



**D** SIV+ vs. SIV-

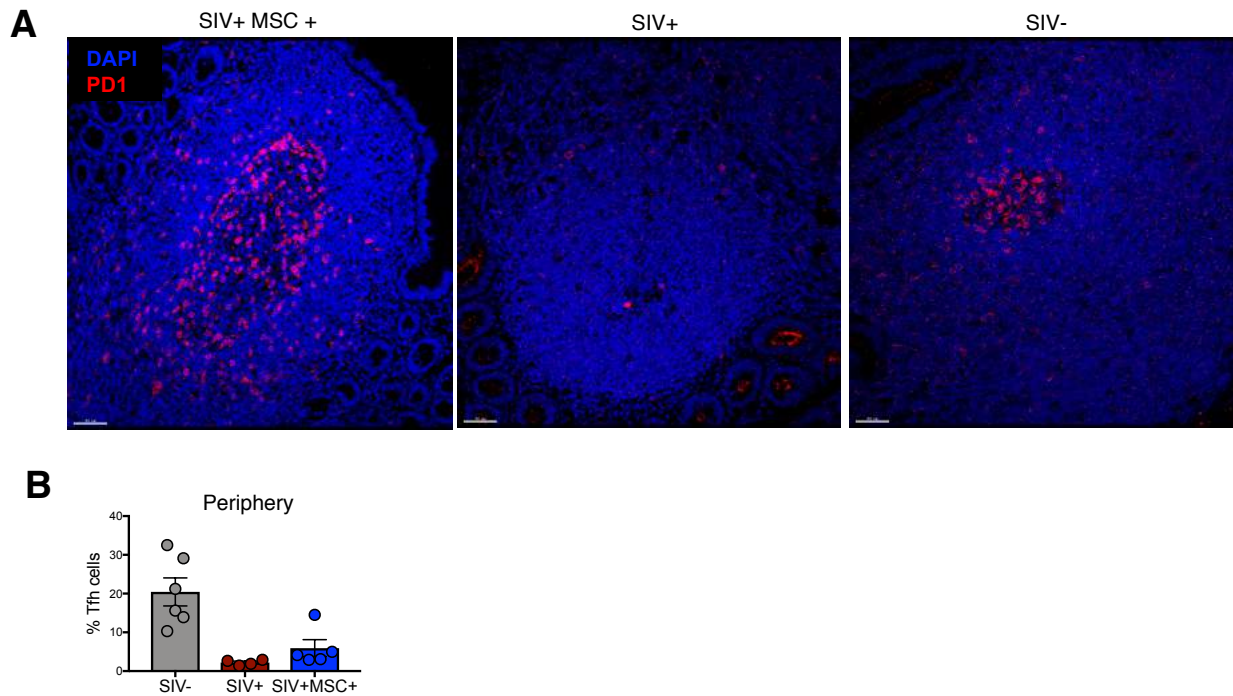
MCODE	Pathway/Description	Log10(P)
1	IFN- $\alpha/\beta$ signaling	-26.3
	Type-1 IFN signaling	-24.9
	Cellular response to type-1 IFN	-24.9
2	ISG15 antiviral mechanism	-10.4
	Antiviral mechanism by IFN-stimulated genes	-10.2
3	IFN signaling	-8.6
	Allograft rejection	-7.5
	Peptide-ligand binding receptors	-6.4
	Positive regulation of transmembrane transport	-6.4

**E**



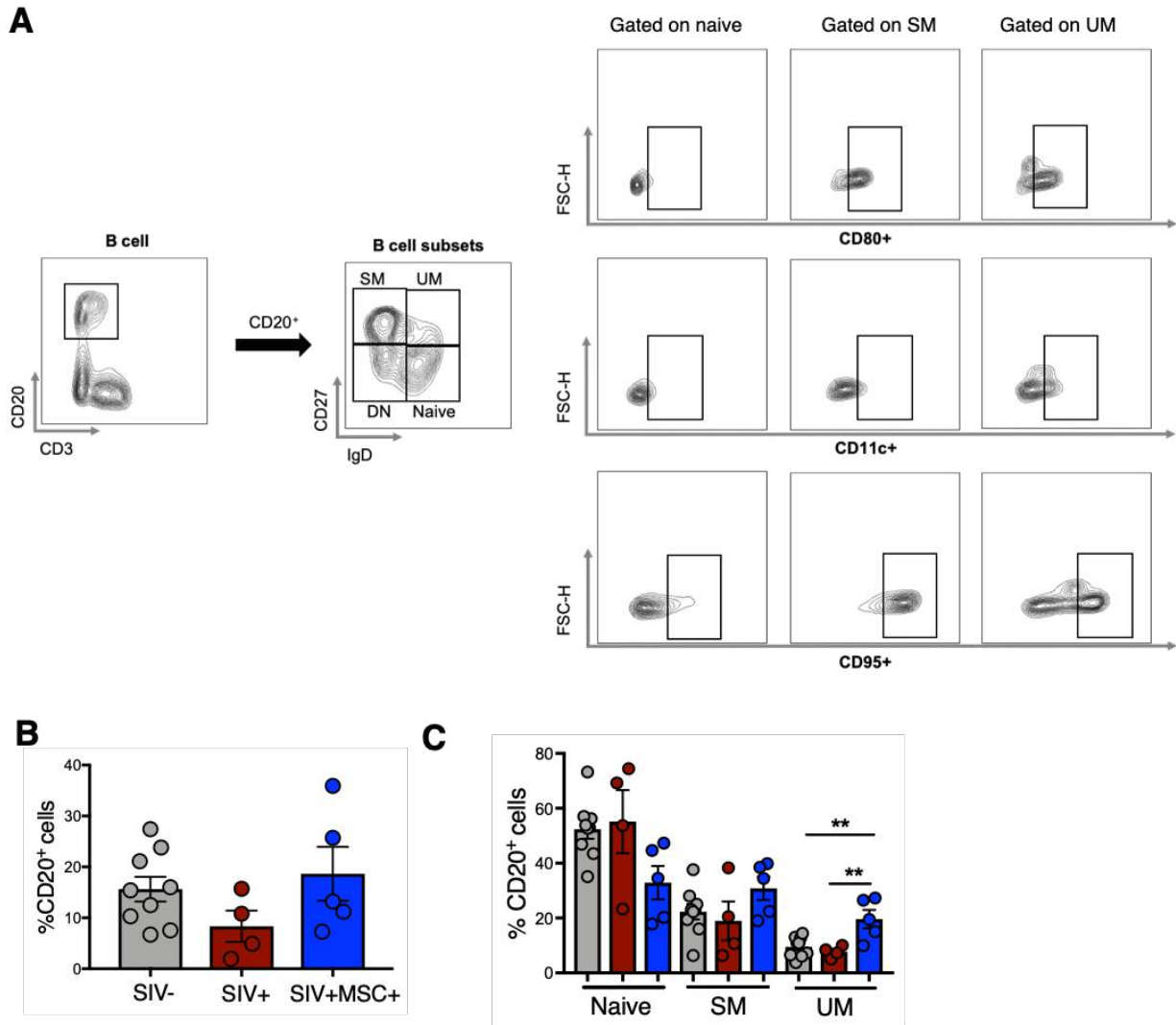
**Supplementary Figure 2. Gut mucosal gene expression signature associated with MSC-treated SIV infected macaques. (A and B) Bar graphs show enriched down-regulated biological**

pathways detected where P represents the Benjamini-Hochberg FDR. **(C)** Network analysis showing term enrichment (node size based on gene count) and interactions (edges) between the top 20 detected biological pathways (color). **(D)** Table displays enriched MCODE modules as determined by a protein-protein interaction analysis. **(E)** Expressed proteins with known physical interactions, associations and biological regulation from enriched modules. All analyses and figures were generated through Metascape.org. Significant down-regulated DEGs from SIV+MSC+ vs. SIV- and SIV+ vs. SIV- animals were used as input to evaluate the magnitude of mucosal antiviral immunity following MSC administration.



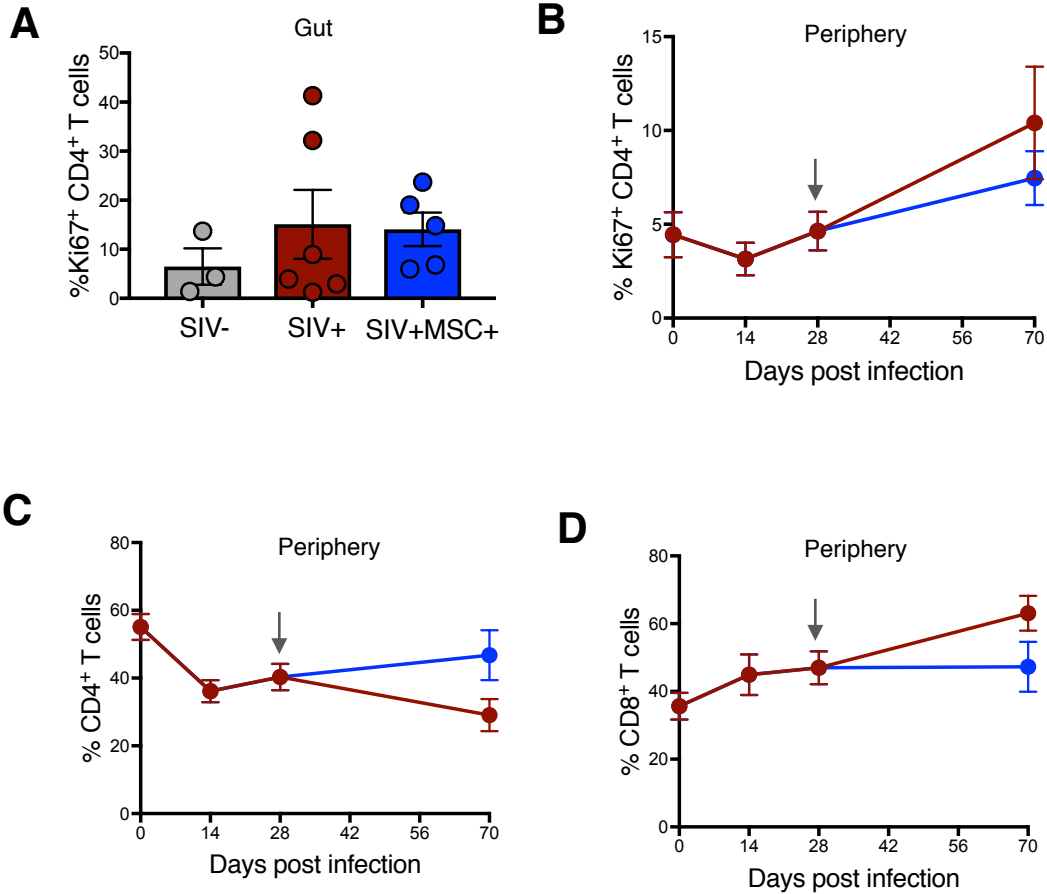
**Supplementary Figure 3. Detection of PD-1+ T expression in gut lymphoid follicles (A)**

Immunohistochemical analysis of PD-1+ expressing cells within ileal lymphoid follicles from representative SIV-, SIV+ and SIV+MSC+ macaques at 70 dpi. Gut sections show nuclei (blue), and anti-PD-1 (red) in the lymphoid follicle. Magnification 20x. Scale bars 50 $\mu$ m. **(B)** Percentage of Tfh (CD4+ CXCR5+) determined by flow cytometry in the peripheral blood (SIV-=6, SIV+n=4, SIV+MSC+n=5).



**Supplementary Figure 4. Flow cytometric gating strategy and B cell subsets in peripheral blood.** (A) Shown are percentages of B cells after gating on lymphocytes, singlets and live cells. B cells were identified by gating on CD3- CD20+ cells. Naïve (CD27- IgD+), switched memory (SM, CD27+ IgD-) and unswitched memory (UM, CD27+ IgD+) were identified by gating on CD27 and IgG. Cells were then gated on CD80, CD11c and CD95. (B and C) Frequency of total B cell (CD3- CD20+), naïve, switched and unswitched B cell populations (SIV-, n=9; SIV+, n =

4; SIV+MSC+, n = 5) at 70 dpi. Significance was determined using the 1-way ANOVA with Holm-Sidak post hoc testing for multiple comparisons (C). \*\* ( $P \leq 0.01$ ).



**Supplementary Figure 5. Detection of T cells subsets.** (A) Percentage of Ki67+ CD4+ T cells at 70 dpi in the colon (SIV- n=3, SIV+ n = 6, SIV+MSC+ n=5). (B-D) Longitudinal frequencies of Ki67+ CD4+ T cells, CD4+ T cells and CD8+ T cells in the periphery at 0, 14, 28 and 70 dpi gut (SIV+ n = 7 and SIV+MSC+ n = 5). Data represent the mean ( $\pm$  SEM) for each time point. Grey arrow represents the first MSC administration.

BIOCHEMICAL	log2fc SIV+/SIV-	p.value	q.value
equol sulfate	-5.217732482	0.002625418	0.141441655
lithocholate	-2.932070097	0.047654433	0.173975112
glutarate (C5-DC)	-2.706905966	0.048814512	0.173975112
heneicosapentaenoate (21:5n3)	-2.620059518	0.005975086	0.141441655
dodecanedioate (C12)	-2.617733563	0.012821685	0.141441655
N-acetyltryptophan	-2.23424581	0.020106576	0.163434898
cinnamoylglycine	-2.17719144	0.008159341	0.141441655
N-octanoylglycine	-2.073713503	0.017445605	0.16249916
docosahexaenoate (DHA; 22:6n3)	-2.008335692	0.011068407	0.141441655
10-undecenoate (11:1n1)	-1.951916855	0.00263701	0.141441655
valylglycine	-1.948219691	0.041745771	0.173928856
indoleacetylglutamine	-1.788619659	0.047937309	0.173975112
3-hydroxydecanoate	-1.739257929	0.043170587	0.173928856
eicosapentaenoate (EPA; 20:5n3)	-1.719526249	0.007003571	0.141441655
cis-4-decenoate (10:1n6)*	-1.712098214	0.010265927	0.141441655
2'-deoxyuridine	-1.693470996	0.006429544	0.141441655
docosapentaenoate (n6 DPA; 22:5n6)	-1.662201533	0.008180663	0.141441655
3-hydroxyoctanoate	-1.618034476	0.040539678	0.173928856
N-acetylaspartate (NAA)	-1.563719889	0.048814512	0.173975112
4-oxo-retinoic acid	-1.559311601	0.004841805	0.141441655
linolenate (18:3n3 or 3n6)	-1.550540301	0.012821685	0.141441655
3-bromo-5-chloro-2,6-dihydroxybenzoic acid*	-1.533123721	0.007016199	0.141441655
stearidonate (18:4n3)	-1.500334508	0.010979131	0.141441655
retinal	-1.500116264	0.019627115	0.16249916
3-hydroxymyristate	-1.494956865	0.033524	0.169683493
5-dodecenoate (12:1n7)	-1.490028363	0.025784235	0.16825866
arachidonate (20:4n6)	-1.474986858	0.007016199	0.141441655
dihomolinoleate (20:2n6)	-1.464341579	0.012821685	0.141441655
(16 or 17)-methylstearate (a19:0 or i19:0)	-1.448326748	0.017869873	0.16249916
lactobacillic acid	-1.426189881	0.012781783	0.141441655
3-hydroxystearate	-1.4040713	0.01683404	0.16249916
hexanoylglycine (C6)	-1.381922053	0.022471077	0.16825866
dihomolinolenate (20:3n3 or 3n6)	-1.343496804	0.012821685	0.141441655
myristoylcarnitine (C14)	-1.332193676	0.048814512	0.173975112
caprate (10:0)	-1.316021764	0.022501067	0.16825866
1-myristoyl-2-arachidonoyl-GPC (14:0/20:4)*	-1.295012842	0.008187777	0.141441655
1-linoleoyl-GPI* (18:2)*	-1.258525751	0.01964073	0.16249916
indoleacetate	-1.25568594	0.025784235	0.16825866
margarate (17:0)	-1.234022619	0.022531072	0.16825866
10-heptadecenoate (17:1n7)	-1.227315939	0.038088284	0.169683493
trans-2-hexenoylglycine	-1.215501918	0.023952962	0.16825866
2-palmitoyl-GPC* (16:0)*	-1.212316702	0.01964073	0.16249916
1-stearoyl-GPI (18:0)	-1.205428585	0.019586293	0.16249916
3,5-dichloro-2,6-dihydroxybenzoic acid	-1.175510371	0.025784235	0.16825866
1-linolenoyl-GPC (18:3)*	-1.169232287	0.033524	0.169683493
2-hydroxypalmitate	-1.156585948	0.011068407	0.141441655
3beta-hydroxy-5-cholestenoate	-1.150787074	0.038002593	0.169683493
stearate (18:0)	-1.146188899	0.011068407	0.141441655
undecenoylcarnitine (C11:1)	-1.140726018	0.038002593	0.169683493
2-hydroxynervonate*	-1.131843318	0.047937309	0.173975112
2-hydroxybehenate	-1.103638724	0.023561682	0.16825866
myristate (14:0)	-1.081039113	0.038088284	0.169683493
dodecadienoate (12:2)*	-1.069933394	0.033524	0.169683493
linoleate (18:2n6)	-1.069218441	0.029435937	0.169683493
octadecanedioate (C18)	-1.061882165	0.038088284	0.169683493
3-(3-hydroxyphenyl)propionate	-1.056419535	0.025718328	0.16825866
sphingomyelin (d17:1/14:0, d16:1/15:0)*	-1.033577356	0.029435937	0.169683493
1-palmitoleoyl-GPC* (16:1)*	-1.023341089	0.033524	0.169683493
oleate/vaccenate (18:1)	-1.023001894	0.025784235	0.16825866
2-hydroxystearate	-1.017932413	0.00368678	0.141441655
3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	-1.015852984	0.014816378	0.159644922
docosadienoate (22:2n6)	-1.01133176	0.033445231	0.169683493
adrenate (22:4n6)	-1.00847747	0.027540699	0.169683493
(14 or 15)-methylpalmitate (a17:0 or i17:0)	-1.007676789	0.038088284	0.169683493
3-hydroxyhexanoate	-0.93741855	0.029435937	0.169683493
hydroxy-CMPF*	-0.936166241	0.007016199	0.141441655
dihomo-linolenoyl-choline	-0.932100444	0.041970859	0.173928856
6-bromotryptophan	-0.930303198	0.02880637	0.169683493

palmitate (16:0)	-0.926001328	0.017079637	0.16249916
eicosanedioate (C20-DC)	-0.910346154	0.025784235	0.16825866
cysteinylglycine	-0.8863994	0.00511391	0.141441655
1-arachidonoyl-GPC* (20:4)*	-0.881376606	0.038088284	0.169683493
pentadecanoate (15:0)	-0.87683545	0.012821685	0.141441655
arachidate (20:0)	-0.868556834	0.038066857	0.169683493
cysteine sulfinic acid	-0.845540264	0.012811704	0.141441655
pyridoxate	-0.828002344	0.048814512	0.173975112
1-stearoyl-GPC (18:0)	-0.81368143	0.011068407	0.141441655
1-stearoyl-2-linoleoyl-GPI (18:0/18:2)	-0.796255449	0.007016199	0.141441655
sphingomyelin (d18:2/21:0, d16:2/23:0)*	-0.780291475	0.043077674	0.173928856
sphingomyelin (d18:2/14:0, d18:1/14:1)*	-0.777040495	0.038088284	0.169683493
1-(1-enyl-stearoyl)-GPE (P-18:0)*	-0.768343688	0.048814512	0.173975112
linoleoylcarnitine (C18:2)*	-0.755565257	0.048814512	0.173975112
3-methylcrotonylglycine	-0.754451132	0.043170587	0.173928856
cys-gly, oxidized	-0.738430708	0.038088284	0.169683493
1-(1-enyl-stearoyl)-2-arachidonoyl-GPE (P-18:0/20:4)*	-0.724604079	0.029435937	0.169683493
1-linoleoyl-2-arachidonoyl-GPC (18:2/20:4n6)*	-0.718814669	0.033524	0.169683493
retinol (Vitamin A)	-0.715690622	0.038088284	0.169683493
tryptophan	-0.695028261	0.012821685	0.141441655
threonate	-0.694885603	0.038088284	0.169683493
citulline	-0.642531904	0.005997428	0.141441655
1-stearoyl-2-docosahexaenoyl-GPC (18:0/22:6)	-0.632366725	0.003690585	0.141441655
methylsuccinate	-0.61970496	0.00511391	0.141441655
5-methyluridine (ribothymidine)	-0.612962425	0.000751428	0.141441655
gamma-tocopherol/beta-tocopherol	-0.606169779	0.048814512	0.173975112
isocitrate	-0.586800664	0.043077674	0.173928856
aconitate [cis or trans]	-0.564952449	0.017079637	0.16249916
1-stearoyl-2-arachidonoyl-GPI (18:0/20:4)	-0.544940948	0.005997428	0.141441655
3-hydroxyindolin-2-one sulfate	0.546711948	0.032621784	0.169683493
1-carboxyethylphenylalanine	0.645307439	0.043170587	0.173928856
5,6-dihydrothymine	0.710683085	0.033524	0.169683493
3-ureidoisobutyrate	0.791542981	0.043147355	0.173928856
formiminoglutamate	0.821648995	0.033524	0.169683493
indolin-2-one	0.950843086	0.04856357	0.173975112
picolinate	1.00427424	0.011068407	0.141441655
N-acetylputrescine	1.004901066	0.017079637	0.16249916
3-ureidopropionate	1.058330318	0.011068407	0.141441655
N-acetyl-1-methylhistidine*	1.072934337	0.005997428	0.141441655
glycerol 3-phosphate	1.100730961	0.022531072	0.16825866
kynurenine	1.151278114	0.001563119	0.141441655
anthranilate	1.271902544	0.008046101	0.141441655
quinolinate	1.488138954	0.005997428	0.141441655
N-formylanthranilic acid	1.492824658	0.043170587	0.173928856
urate	1.664740426	0.008187777	0.141441655
3-methoxytyramine sulfate	3.508192085	0.026507093	0.169683493
glycochenodeoxycholate glucuronide (1)	4.783895949	0.045500264	0.173975112
2,3-dihydroxyisovalerate	4.865244142	0.030514659	0.169683493
carnosine	5.24654175	0.043170587	0.173928856

**Supplementary Table 1.** Significantly increased metabolites following SIV infection.



BIOCHEMICAL	log2fc SIV+MSC+/SIV+	p.value	q.value
carnosine	-7.481601691	0.028459737	0.074378169
3-methoxytyramine sulfate	-5.996513323	0.017365464	0.061799624
2,3-dihydroxyisovalerate	-5.490208715	0.049745991	0.103611059
4-acetamidobenzoate	-4.656082984	0.049745991	0.103611059
heme	-2.929626822	0.017622091	0.061799624
2-pyrrolidinone	-2.796731623	0.016604954	0.061799624
suberoylcarnitine (C8-DC)	-2.740783881	0.042680184	0.094350021
picolinate	-2.426197789	0.006169899	0.061183519
leucylhydroxyproline*	-2.012967128	0.034463821	0.089499495
2-hydroxyheptanoate*	-1.941549461	0.017622091	0.061799624
1-carboxyethylisoleucine	-1.767752299	0.006169899	0.061183519
indoleacetyl carnitine*	-1.762487816	0.028459737	0.074378169
1-carboxyethylvaline	-1.753070354	0.006169899	0.061183519
N-acetyl-1-methylhistidine*	-1.751185545	0.017622091	0.061799624
octadecenedioylcarnitine (C18:1-DC)*	-1.740100966	0.028459737	0.074378169
tiglyl carnitine (C5)	-1.709954315	0.006169899	0.061183519
2S,3R-dihydroxybutyrate	-1.66735092	0.017622091	0.061799624
2-aminobutyrate	-1.660025582	0.006169899	0.061183519
N,N,N-trimethyl-alanylproline betaine (TMAP)	-1.631452879	0.006169899	0.061183519
alpha-hydroxyisovalerate	-1.626522448	0.006169899	0.061183519
propionylcarnitine (C3)	-1.617858436	0.010587137	0.061183519
N-acetyl-aspartyl-glutamate (NAAG)	-1.538713286	0.017622091	0.061799624
lanthionine	-1.520176575	0.042680184	0.094350021
alpha-hydroxyisocaproate	-1.495161632	0.006053705	0.061183519
2-hydroxy-3-methylvalerate	-1.444446422	0.006053705	0.061183519
N-acetylneuraminic acid	-1.430568227	0.027030077	0.074378169
gamma-glutamyl-2-aminobutyrate	-1.405759686	0.028459737	0.074378169
gamma-glutamylmethionine	-1.369458037	0.044609718	0.094350021
bilirubin	-1.265786576	0.006169899	0.061183519
alpha-ketobutyrate	-1.25817073	0.010411098	0.061183519
octadecanedioylcarnitine (C18-DC)*	-1.251747669	0.044609718	0.094350021
beta-hydroxyisovaleroylcarnitine	-1.239832209	0.028459737	0.074378169
biliverdin	-1.226789656	0.017622091	0.061799624
beta-alanine	-1.218418548	0.028459737	0.074378169
2-hydroxybutyrate/2-hydroxyisobutyrate	-1.213676571	0.028459737	0.074378169
arabitol/xylitol	-1.212374267	0.028459737	0.074378169
malonylcarnitine	-1.191391133	0.010587137	0.061183519
butyrylcarnitine (C4)	-1.169700297	0.028459737	0.074378169
2-methylbutyrylcarnitine (C5)	-1.159026908	0.010587137	0.061183519
N-acetylputrescine	-1.152255257	0.044609718	0.094350021
threonine	-1.061843235	0.006169899	0.061183519
isobutyrylcarnitine (C4)	-1.03549576	0.006169899	0.061183519
creatine	-1.026617677	0.006169899	0.061183519
deoxycarnitine	-1.015168155	0.017622091	0.061799624
alanine	-0.96189517	0.006169899	0.061183519
gamma-glutamylthreonine	-0.951338239	0.028459737	0.074378169
fructosyllysine	-0.947538844	0.028459737	0.074378169
hydroxyproline	-0.888460936	0.010587137	0.061183519
1-carboxyethylleucine	-0.881190596	0.044609718	0.094350021
hydroxy-N6,N6,N6-trimethyllysine*	-0.873878131	0.028459737	0.074378169
nonanoylcarnitine (C9)	-0.86470595	0.017622091	0.061799624
asparagine	-0.847075066	0.006169899	0.061183519
N6-carbamoylthreonyladenosine	-0.807296888	0.042680184	0.094350021
methionine	-0.774444641	0.006169899	0.061183519
N-acetylglucosamine/N-acetylgalactosamine	-0.764669543	0.006169899	0.061183519
gamma-glutamylvaline	-0.753371499	0.044609718	0.094350021
carnitine	-0.74704285	0.017622091	0.061799624
1,2-dipalmitoyl-GPC (16:0/16:0)	-0.669233733	0.028459737	0.074378169
gamma-glutamylhistidine	-0.660160058	0.028459737	0.074378169
3-hydroxyisobutyrate	-0.654025137	0.044609718	0.094350021
N-acetyl-isoptureanine	-0.647633587	0.017622091	0.061799624
valine	-0.646120684	0.044609718	0.094350021
gamma-glutamylphenylalanine	-0.634938628	0.017622091	0.061799624
gamma-glutamyltyrosine	-0.618567752	0.044609718	0.094350021
histidine	-0.584800649	0.017622091	0.061799624
ribitol	-0.570876034	0.017622091	0.061799624
1-palmitoyl-2-docosahexaenoyl-GPE (16:0/22:6)*	0.54620997	0.044609718	0.094350021
behenoyl sphingomyelin (d18:1/22:0)*	0.576476202	0.044609718	0.094350021
1-stearoyl-2-oleoyl-GPC (18:0/18:1)	0.593015043	0.044609718	0.094350021
1-stearoyl-2-linoleoyl-GPE (18:0/18:2)*	0.647039666	0.028459737	0.074378169

carotene diol (2)	0.657431522	0.044609718	0.094350021
methylsuccinate	0.660088925	0.017622091	0.061799624
4-hydroxyphenylpyruvate	0.668623387	0.044609718	0.094350021
lignoceroyl sphingomyelin (d18:1/24:0)	0.677633096	0.044609718	0.094350021
1-stearoyl-2-arachidonoyl-GPI (18:0/20:4)	0.68512921	0.006169899	0.061183519
1-arachidonoyl-GPE (20:4n6)*	0.690625367	0.044609718	0.094350021
glutamate	0.708462343	0.044609718	0.094350021
sphingomyelin (d18:1/14:0, d16:1/16:0)*	0.741322178	0.010587137	0.061183519
sphingomyelin (d18:2/14:0, d18:1/14:1)*	0.745475529	0.044609718	0.094350021
3,5-dichloro-2,6-dihydroxybenzoic acid	0.757449301	0.028459737	0.074378169
hydroxy-CMPF*	0.793120578	0.017622091	0.061799624
1-oleoyl-2-linoleoyl-GPE (18:1/18:2)*	0.842045939	0.028459737	0.074378169
glycerophosphorylcholine (GPC)	0.914730319	0.044609718	0.094350021
threonate	0.916751037	0.044609718	0.094350021
thyroxine	0.934942882	0.044609718	0.094350021
1-(1-enyl-stearoyl)-2-oleoyl-GPE (P-18:0/18:1)	0.95457994	0.017622091	0.061799624
1-oleoyl-2-docosahexaenoyl-GPC (18:1/22:6)*	0.987259558	0.010587137	0.061183519
1-(1-enyl-stearoyl)-2-linoleoyl-GPE (P-18:0/18:2)*	0.987837003	0.017622091	0.061799624
1-palmitoyl-GPC (16:0)	0.992351032	0.028459737	0.074378169
1-(1-enyl-palmitoyl)-GPE (P-16:0)*	1.010818047	0.017622091	0.061799624
3-methylcrotonylglycine	1.012915561	0.017622091	0.061799624
butyrylglycine (C4)	1.059320736	0.017622091	0.061799624
1-arachidonoyl-GPC* (20:4)*	1.062663696	0.010587137	0.061183519
homoarginine	1.118585989	0.006169899	0.061183519
1-stearoyl-GPE (18:0)	1.134704936	0.028459737	0.074378169
3-bromo-5-chloro-2,6-dihydroxybenzoic acid*	1.160359117	0.010587137	0.061183519
cysteine sulfinic acid	1.169877918	0.028100064	0.074378169
1-linoleoyl-2-arachidonoyl-GPC (18:2/20:4n6)*	1.199266181	0.006169899	0.061183519
1-linoleoyl-GPC (18:2)	1.228041289	0.028459737	0.074378169
2-hydroxypalmitate	1.258430985	0.044609718	0.094350021
1-(1-enyl-palmitoyl)-GPC (P-16:0)*	1.272501259	0.028459737	0.074378169
1-oleoyl-GPC (18:1)	1.286746681	0.028459737	0.074378169
1-myristoyl-2-arachidonoyl-GPC (14:0/20:4)*	1.295683523	0.028459737	0.074378169
1-palmitoleoyl-2-linolenoyl-GPC (16:1/18:3)*	1.335383433	0.017622091	0.061799624
2-hydroxystearate	1.341706284	0.010411098	0.061183519
1-stearoyl-2-linoleoyl-GPI (18:0/18:2)	1.357494429	0.006169899	0.061183519
1,2-dilinoleoyl-GPC (18:2/18:2)	1.39196874	0.006169899	0.061183519
phenylacetylglutamine	1.401389153	0.044609718	0.094350021
10-undecenoate (11:1n1)	1.405502892	0.017622091	0.061799624
1-palmitoyl-2-arachidonoyl-GPI (16:0/20:4)*	1.414674318	0.010587137	0.061183519
retinol (Vitamin A)	1.416256615	0.010587137	0.061183519
3-hydroxyhippurate	1.427874504	0.022043575	0.074378169
1-oleoyl-2-docosahexaenoyl-GPE (18:1/22:6)*	1.432828545	0.017622091	0.061799624
phenylacetylglutamine	1.44168396	0.028459737	0.074378169
3beta-hydroxy-5-cholestenate	1.442677825	0.04412557	0.094350021
leucylalanine	1.454436088	0.017365464	0.061799624
1-stearoyl-GPC (18:0)	1.464477836	0.006169899	0.061183519
oleoyl-linoleoyl-glycerol (18:1/18:2) [2]	1.493128794	0.006169899	0.061183519
6-bromotryptophan	1.494618883	0.028100064	0.074378169
palmitoyl-linoleoyl-glycerol (16:0/18:2) [2]*	1.499613849	0.010587137	0.061183519
1-(1-enyl-stearoyl)-GPE (P-18:0)*	1.503862029	0.017622091	0.061799624
1-palmitoyl-2-linoleoyl-GPI (16:0/18:2)	1.510887005	0.006169899	0.061183519
1-palmitoyl-2-oleoyl-GPI (16:0/18:1)*	1.531050876	0.010587137	0.061183519
arachidonate (20:4n6)	1.539182232	0.017622091	0.061799624
1-oleoyl-2-arachidonoyl-GPI (18:1/20:4)*	1.540342259	0.010587137	0.061183519
docosapentaenoate (n6 DPA; 22:5n6)	1.564910216	0.010411098	0.061183519
picolinoylglycine	1.570293955	0.024932456	0.074378169
p-cresol glucuronide*	1.591896431	0.028100064	0.074378169
oleoyl-linoleoyl-glycerol (18:1/18:2) [1]	1.59232199	0.006169899	0.061183519
p-cresol sulfate	1.596099303	0.010587137	0.061183519
dihomolinate (20:3n3 or 3n6)	1.640998438	0.017622091	0.061799624
3-hydroxystearate	1.641611476	0.006053705	0.061183519
3-indoxyl sulfate	1.663004514	0.010587137	0.061183519
palmitoyl-linoleoyl-glycerol (16:0/18:2) [1]*	1.67363603	0.010587137	0.061183519
6-hydroxyindole sulfate	1.674419988	0.017622091	0.061799624
4-oxo-retinoic acid	1.677501427	0.035174861	0.090204178
2-stearoyl-GPE (18:0)*	1.730596619	0.017365464	0.061799624
2-palmitoyl-GPC* (16:0)*	1.763434508	0.010587137	0.061183519
retinal	1.782327675	0.010411098	0.061183519
linoleoyl-linoleoyl-glycerol (18:2/18:2) [1]*	1.789837853	0.006169899	0.061183519
1-linoleoyl-GPA (18:2)*	1.793632323	0.006169899	0.061183519
palmitoyl-oleoyl-glycerol (16:0/18:1) [2]*	1.853941265	0.017622091	0.061799624
1-ribosyl-imidazoleacetate*	1.883247668	0.028459737	0.074378169
N-methylproline	1.930450673	0.017622091	0.061799624
linoleoyl-linolenoyl-glycerol (18:2/18:3) [1]*	1.941226564	0.028459737	0.074378169
1-linoleoyl-2-linolenoyl-GPC (18:2/18:3)*	1.955987792	0.006169899	0.061183519

1-stearoyl-2-oleoyl-GPI (18:0/18:1)*	1.974733913	0.010587137	0.061183519
docosahexaenoate (DHA; 22:6n3)	2.005016062	0.010587137	0.061183519
1-linoleoyl-GPI* (18:2)*	2.027711681	0.010587137	0.061183519
1-linolenoyl-GPC (18:3)*	2.032388012	0.010587137	0.061183519
palmitoyl-oleoyl-glycerol (16:0/18:1) [1]*	2.033937001	0.010587137	0.061183519
oleoyl-oleoyl-glycerol (18:1/18:1) [1]*	2.047781907	0.006169899	0.061183519
1-palmitoleoyl-GPC* (16:1)*	2.069231452	0.010587137	0.061183519
1-stearoyl-GPI (18:0)	2.246094543	0.006169899	0.061183519
oleoyl-oleoyl-glycerol (18:1/18:1) [2]*	2.275772766	0.006169899	0.061183519
palmitoylcholine	2.323572496	0.044609718	0.094350021
1-lignoceroyl-GPC (24:0)	2.332098181	0.028100064	0.074378169
4-allylphenol sulfate	2.339887309	0.027030077	0.074378169
palmitoleoyl-linoleoyl-glycerol (16:1/18:2) [1]*	2.443806894	0.010587137	0.061183519
3-phenylpropionate (hydrocinnamate)	2.464139538	0.04412557	0.094350021
diacylglycerol (16:1/18:2 [2], 16:0/18:3 [1])*	2.498572284	0.010587137	0.061183519
linoleoyl-linolenoyl-glycerol (18:2/18:3) [2]*	2.578432302	0.00734473	0.061183519
heneicosapentaenoate (21:5n3)	2.624217659	0.028100064	0.074378169
1-oleoyl-GPI (18:1)	2.812955637	0.017365464	0.061799624
hippurate	2.91708645	0.028459737	0.074378169
palmitoleoyl-arachidonoyl-glycerol (16:1/20:4) [2]*	3.004934795	0.035174861	0.090204178
1-palmitoyl-GPI* (16:0)	3.03685194	0.010411098	0.061183519
cinnamoylglycine	3.237277871	0.017365464	0.061799624
docosahexaenoylcholine	3.274370086	0.017365464	0.061799624
equol glucuronide	3.484777815	0.011163994	0.061799624
N-acetyltryptophan	3.61102606	0.015127246	0.061799624
deoxycholate	3.679342924	0.017622091	0.061799624
4-methylcatechol sulfate	3.767300958	0.04412557	0.094350021
lithocholate	4.032029996	0.011163994	0.061799624
dihomo-linolenoyl-choline	4.160179239	0.036571191	0.093202483
indolepropionate	4.597916618	0.017622091	0.061799624
4-ethylphenyl sulfate	5.578175588	0.010411098	0.061183519
equol sulfate	5.876817264	0.016604954	0.061799624

**Supplementary Table 2.** Significantly increased metabolites following MSC administration.

<b>Study Group</b>	<b>Animals/group</b>	<b>Weight (kg)</b>	<b>Sex (F:M)</b>	<b>Age (yrs.)</b>
SIV-	18	9.6 ± 2.3	2:16	6.0 ± 1.9
SIV+	12	9.7 ± 2.8	3:9	8.0 ± 1.1
SIV+MSC+	5	7.2 ± 1.3	5:0	6.8 ± 1.9

**Supplementary Table 3.** Characteristics of animals in the study groups

Antigen/Reagent	Conjugate	Clone	Company	Catalog Number
CD3	Pacific Blue	SP34-2	BD	558124
CD3	AF700	SP-234	BD	557917
CD4	PerPCy5.5	OKT4	Biolegend	317427
CD4	BV650	L200	BD	563737
CD8	PE Dazzle 594	RPA-T8	Biolegend	301057
CD8	PerCPCy5.5	SK1	BD	341049
CD8	BV510	SK1	BD	563919
CD45	AF700	D058-1283	BD	561288
Ki67	AF488	B56	Fisher Scientific	BDB561165
CD95	APC	DX2	BD	558814
CD95	BUV737	DX2	BD	564710
CXCR5	PE	MU5UBEE	Invitrogen	12-9185-411G1
CXCR5	BV421	MU5BEE	Invitrogen	48-9185-4
PD-1	PECyanine7	EH12.2H7	Biolegend	329918
Granzyme B	PECF594	GB11	BD	562462
CD20	BV421	2H7	Biolegend	302328
CD20	APC-H7	L27	BD	641396
CD11c	BV650	S-HCL-3	BD	744437
CD21	PECyanine7	B-ly4	BD	561374
CD27	Pacific Blue	M-T271	Biolegend	356413
CD80	PE	L307-4	BD	557227
IgD	FITC		Southern Biotech	2030-02
IFN $\gamma$	PECyanine7	B27	BD	557643
TNF- $\alpha$	AF488	Mab11	Invitrogen	53-734971
Live-dead marker	APCCy7	NA	Invitrogen	L34976A
Live-dead marker	Aqua	NA	Invitrogen	L34957

**Supplementary Table 4.** Flow cytometry reagents.