

Supplementary Materials for

**Immunoregulatory and lipid presentation pathways are upregulated in human face  
transplant rejection**

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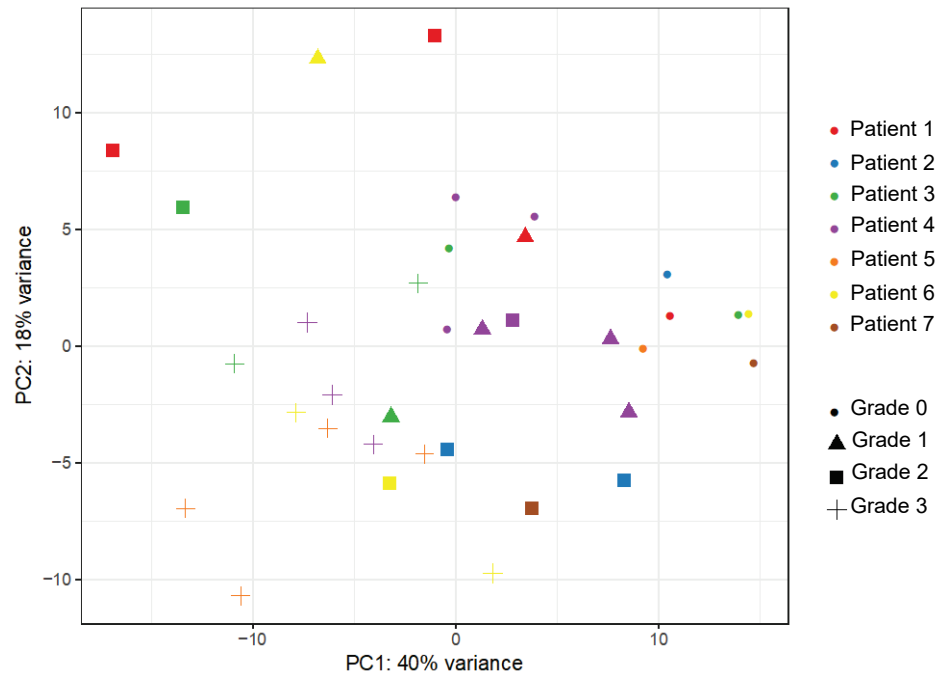
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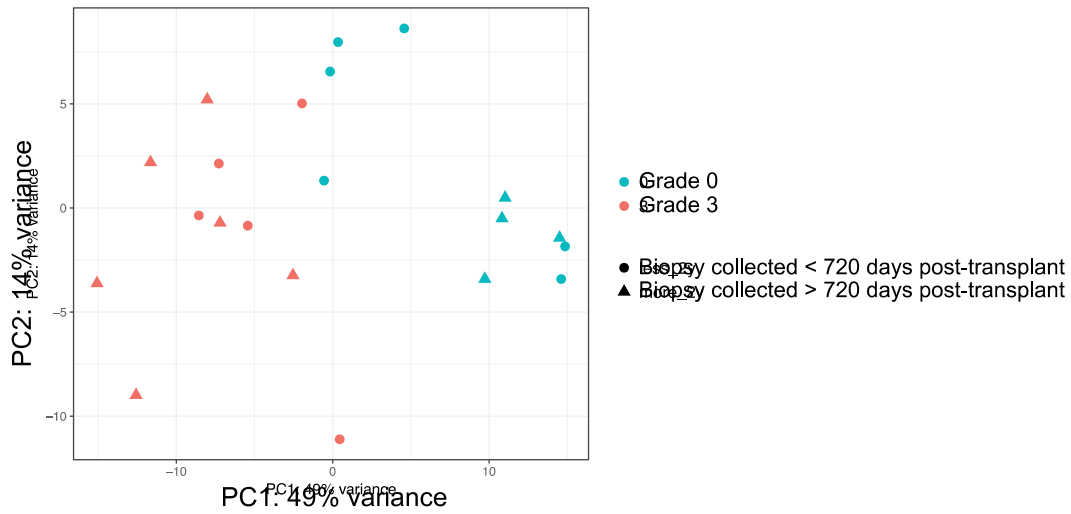
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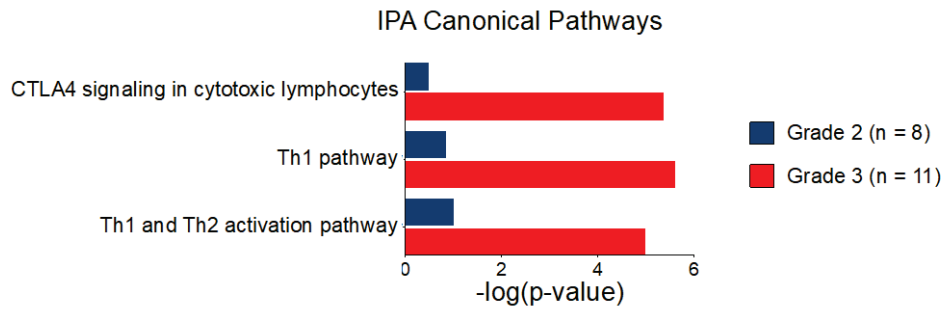


**Supplementary Figure 1. Principal component analysis revealed that the samples clustered on the basis of rejection status.**

Unsupervised principal component analysis of all allograft biopsies (n = 35) included in the analyses of the study revealed that the samples clustered on the basis of rejection status irrespective of the origin of the biopsies.

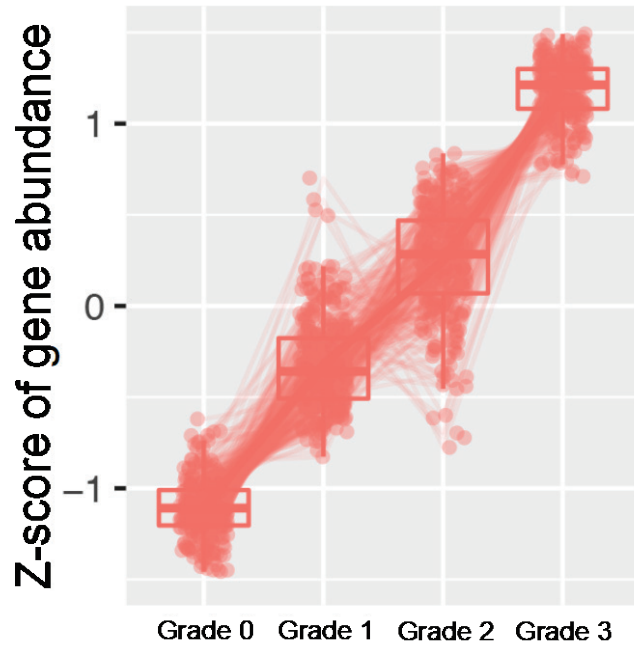


**Supplementary Figure 2. Biopsies did not cluster on the basis of the time of biopsy collection.** Unsupervised principal component analysis revealed that the biopsy samples (Grade 0, n = 10; Grade 3, n = 11) clustered on the basis of rejection status irrespective of the time of biopsy collection from transplantation.



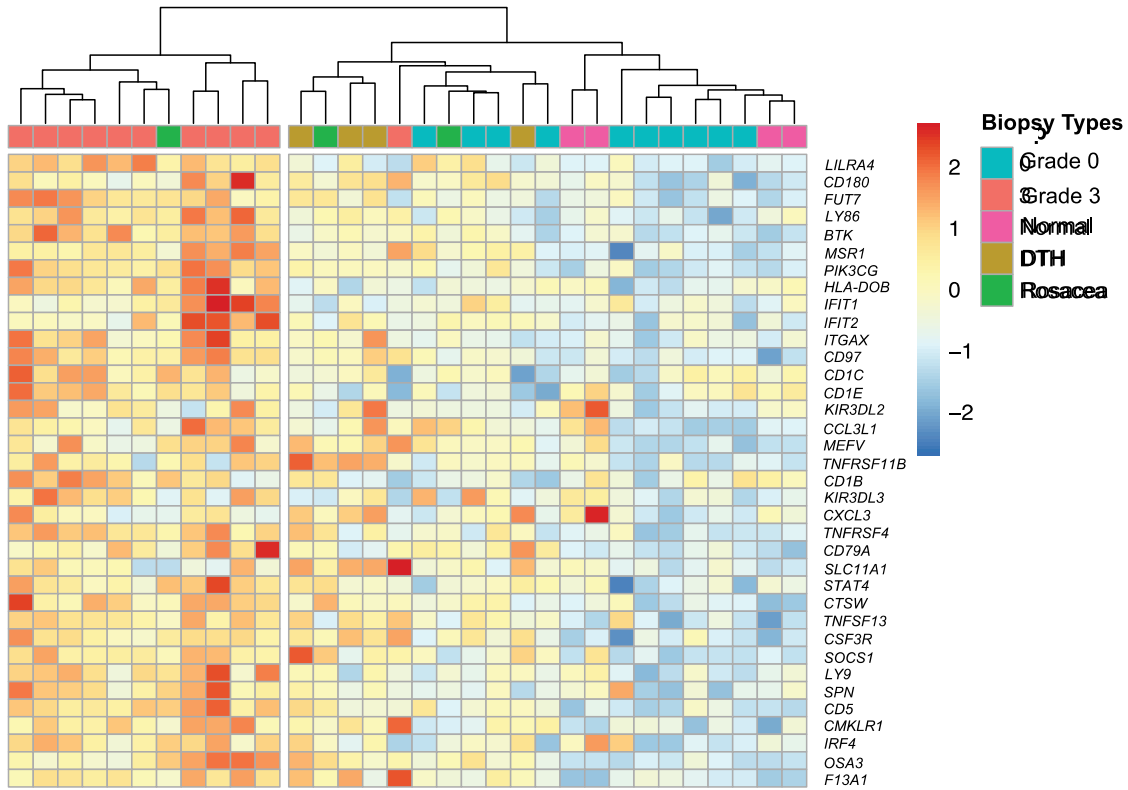
**Supplementary Figure 3. Ingenuity pathway analysis identified progressive enrichment of T cell associated pathways with increasing severity of rejection.**

Benjamini-Hochberg corrected Fischer's exact test P values are shown.



**Supplementary Figure 4. Pattern of increased expression correlating with rejection grade for a cluster of 273 genes, differentially expressed across rejection grades.**

The x-axis represents the Banff rejection grades [Grade 0 (n = 10); Grade 1 (n = 6); Grade 2 (n = 8); Grade 3 (n = 11)] and the y-axis, the centered and scaled expression for the genes (equivalent to z-score). The complete list of 273 genes is shown in Supplementary Table 8.



**Supplementary Figure 5. Heatmap of normalized expression values for thirty-six genes upregulated in face transplant rejection that have not been reported in solid organ transplant rejection.**

The complete list of the thirty-six genes is detailed in Supplementary Table 13. Each column represents a biopsy sample. Gene expression row scaled. The cell color represents normalized levels from high (red) to middle (yellow) to low (blue). The degree of relatedness is represented by the dendrogram at the top of the panel (unsupervised hierarchical clustering). All except one biopsy collected from non-transplanted patients with rosacea clustered separately from rejection (Banff Grade 3) samples.

**Supplementary Table 1. Donor and recipient characteristics.**

Recipient characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
<b>Age at transplant (years)</b>	57	25	30	44	59	38	33
<b>Gender</b>	Female	Male	Male	Female	Male	Male	Male
<b>Mechanism of injury</b>	Animal bite	Electrical burn	Electrical burn	Chemical burn	Electrical burn	Gunshot	Gunshot
<b>Year of transplant</b>	2011	2011	2011	2013	2009	2014	2014
<b>Follow-up (months)</b>	89	91	90	68	114	55	48
<b>Facial allograft details</b>	Full face	Full face	Full face	Full face	Partial face	Partial face	Partial face
<b>Panel reactive antibodies (%)</b>	0	68	0	97	0	22	32
<b>Donor specific antibodies</b>	Negative	Negative	Negative	Positive	Negative	Negative	Negative
<b>HLA mismatch (A, B, C, DR, DQ, DP)</b>	8	8	5	11	4	8	7
<b>CMV status</b>	Positive	Positive	Negative	Positive	Positive	Negative	Positive
<b>EBV status</b>	Positive	Positive	Positive	Positive	Positive	Positive	Positive
<b>Induction therapy</b>	ATG 1.5mg/kg/day x4; high dose steroids	ATG 1.5mg/kg/day x4; high dose steroids	ATG 1.5mg/kg/day x4; high dose steroids	ATG 1.5mg/kg/day x4; MMF 2g/day; tacrolimus 4mg/day; high dose steroids*	ATG 1.5mg/kg/day x3; high dose steroids	ATG 1.5mg/kg/day x2/0.75mg/kg/day x2; high dose steroids	ATG 1.5mg/kg/day x3; high dose steroids
<b>Donor characteristics</b>							
<b>Age (years)</b>	42	48	31	56	55	51	23
<b>Gender</b>	Female	Male	Male	Female	Male	Male	Male
<b>CMV status</b>	Positive	Positive	Positive	Negative	Positive	Positive	Negative
<b>EBV status</b>	Positive	Positive	Positive	Positive	Positive	Positive	Positive
<b>Ischemia time (minutes)</b>	120	240	120	180	150	180	90

\*Patient 4 was highly sensitized and therefore, received additional immunosuppressants alongside the standard induction regimen with rabbit anti-thymocyte globulin (ATG) as previously reported (1). HLA, human leukocyte antigen; MMF, mycophenolate mofetil; CMV, cytomegalovirus; EBV, Epstein-Barr virus.

**Supplementary Table 2. Histological and clinical characteristics of allograft skin biopsy samples included in the analyses of the study.**

Sample No.	Patient	Banff Grade	Immunosuppressive regime at time of biopsy	Treatment of acute rejection
1	Patient 1	2	Tacrolimus, MMF	Tacrolimus dose increased
2	Patient 1	1	Tacrolimus, MMF	None
3	Patient 1	0	Tacrolimus, MMF	NA
4	Patient 1	2	Tacrolimus, MMF	None
5	Patient 2	2	Tacrolimus, MMF	Oral glucocorticoids, anti-thymocyte globulin
6	Patient 2	0	Tacrolimus, MMF	NA
7	Patient 2	2	Tacrolimus, MMF	Oral glucocorticoids
8	Patient 3	2	Tacrolimus, MMF, maintenance glucocorticoid	Glucocorticoid pulse <sup>A</sup> , Tacrolimus dose increased
9	Patient 3	1	Tacrolimus, MMF, maintenance glucocorticoid	None
10	Patient 3	0	Tacrolimus, MMF	NA
11	Patient 3	3	Tacrolimus, MMF	Glucocorticoid pulse <sup>A</sup> , Tacrolimus and MMF doses increased
12	Patient 3	3	Tacrolimus, MMF	Glucocorticoid pulse <sup>A</sup>
13	Patient 3	0	Tacrolimus, MMF	NA
14	Patient 4	0	Tacrolimus, MMF, maintenance glucocorticoid	NA
15	Patient 4	0	Tacrolimus, MMF, maintenance glucocorticoid	NA
16	Patient 4	1	Tacrolimus, MMF, maintenance glucocorticoid	None
17	Patient 4	0	Tacrolimus, MMF, maintenance glucocorticoid	NA
18	Patient 4	3	Tacrolimus, MMF, maintenance glucocorticoid	Glucocorticoid pulse <sup>A</sup>
19	Patient 4	3	Tacrolimus, MMF, maintenance glucocorticoid	Oral glucocorticoids
20	Patient 4	1	Tacrolimus, MMF, maintenance glucocorticoid	None
21	Patient 4	3	Tacrolimus, MMF, maintenance glucocorticoid	Oral glucocorticoids
22	Patient 4	1	Tacrolimus, MMF, maintenance glucocorticoid	None
23	Patient 4	2	Tacrolimus, MMF, maintenance glucocorticoid	None
24	Patient 5	3	Tacrolimus, MMF	Glucocorticoid pulse <sup>A</sup>
25	Patient 5	3	Tacrolimus, MMF, maintenance glucocorticoid	Glucocorticoid pulse <sup>A</sup>
26	Patient 5	3	Tacrolimus, MMF, maintenance glucocorticoid	Glucocorticoid pulse <sup>A</sup> , topical tacrolimus
27	Patient 5	3	Tacrolimus, MMF	Glucocorticoid pulse <sup>A</sup>
28	Patient 5	0	Tacrolimus, MMF	NA
29	Patient 6	3	Tacrolimus, MMF	Glucocorticoid pulse <sup>A</sup>
30	Patient 6	1	Tacrolimus, MMF	None
31	Patient 6	2	Tacrolimus, MMF	Glucocorticoid pulse <sup>A</sup>
32	Patient 6	0	Tacrolimus, MMF	NA
33	Patient 6	3	Tacrolimus, MMF	Glucocorticoid pulse <sup>A</sup>
34	Patient 7	2	Tacrolimus, MMF, maintenance glucocorticoid	Glucocorticoid pulse <sup>A</sup>
35	Patient 7	0	Tacrolimus, MMF	NA



<sup>A</sup> Glucocorticoid pulse treatment consisted of 3 days course of intravenous methylprednisolone.

MMF, mycophenolate mofetil; NA, not applicable.

**Supplementary Table 3. List of the 202 significantly differentially expressed genes in Grade 3 biopsies compared to Grade 0 biopsies.**

Differentially expressed genes ( $\log_2$  fold change  $> 1$ ; adjusted p value  $< 0.05$ ) in Grade 3 (n = 11) compared to Grade 0 (n = 10) were evaluated by the Wald test, using the R package DESeq2-v.1.20.0. P values were adjusted using Benjamini-Hochberg procedure.

Gene Symbol	Log2 Fold Change	Adjusted p value
GZMB	3.408399293	2.44E <sup>-14</sup>
CXCL10	3.254782936	7.73E <sup>-09</sup>
CXCL9	3.018622816	1.54E <sup>-08</sup>
CCL18	2.492905496	1.02E <sup>-05</sup>
IDO1	2.345913685	4.38E <sup>-09</sup>
C1QB	2.28873685	8.12E <sup>-07</sup>
CXCR3	2.257045809	1.42E <sup>-10</sup>
LAG3	2.229244219	1.24E <sup>-10</sup>
CXCL11	2.039479683	1.21E <sup>-05</sup>
IL2RG	2.036657811	3.61E <sup>-11</sup>
XCL2	2.027650828	5.73E <sup>-08</sup>
FCGR3A	2.024118189	6.86E <sup>-08</sup>
ISG15	2.022203685	2.99E <sup>-06</sup>
CLEC4C	2.005658346	2.42E <sup>-05</sup>
IRF8	1.995988235	7.12E <sup>-10</sup>
HLA-DRA	1.969404649	2.23E <sup>-11</sup>
CD3D	1.938555344	2.29E <sup>-10</sup>
CTSS	1.894946302	4.84E <sup>-12</sup>
LTB	1.889930162	3.61E <sup>-05</sup>
GZMK	1.889537791	2.71E <sup>-08</sup>
CD2	1.885599484	4.01E <sup>-08</sup>
CD8A	1.884316831	2.71E <sup>-08</sup>
GNLY	1.882614297	4.46E <sup>-05</sup>
C1QA	1.861448083	1.09E <sup>-07</sup>
CD163	1.857206159	2.17E <sup>-06</sup>
CD53	1.829408761	1.01E <sup>-11</sup>
PTPRC	1.823290478	9.13E <sup>-13</sup>
CCR1	1.817694789	5.10E <sup>-07</sup>
CCL4	1.799557075	2.11E <sup>-06</sup>
HLA-DPB1	1.794999976	3.70E <sup>-14</sup>
SELPLG	1.793854415	9.01E <sup>-16</sup>
TNFRSF4	1.790937255	1.58E <sup>-06</sup>
CTLA4	1.78880823	5.18E <sup>-06</sup>
SH2D1A	1.775909849	3.83E <sup>-09</sup>
PRF1	1.771469169	9.88E <sup>-09</sup>
CD3G	1.763318844	4.01E <sup>-08</sup>
HLA-DOB	1.752992601	1.96E <sup>-08</sup>
GZMA	1.750937452	2.09E <sup>-08</sup>
HLA-DPA1	1.749449127	1.01E <sup>-11</sup>
CCL5	1.742809019	4.08E <sup>-07</sup>
LY86	1.728837002	7.25E <sup>-10</sup>
TNFSF13B	1.722516488	6.33E <sup>-08</sup>
CYBB	1.717387747	3.12E <sup>-08</sup>
LAMP3	1.716565652	5.24E <sup>-06</sup>
CD27	1.71537078	1.86E <sup>-07</sup>
STAT1	1.714005729	2.82E <sup>-07</sup>
FCGR2A	1.698741423	1.09E <sup>-09</sup>
LCP1	1.689301726	5.24E <sup>-11</sup>
CD80	1.686424973	7.56E <sup>-04</sup>

CCR5	1.68192851	1.98E <sup>-05</sup>
CD48	1.679219002	1.69E <sup>-07</sup>
CR1	1.675121323	6.60E <sup>-05</sup>
HLA-DQA1	1.673744106	1.31E <sup>-02</sup>
CD83	1.670818169	4.77E <sup>-07</sup>
CXCR6	1.668507932	1.75E <sup>-06</sup>
FCER1G	1.662460795	1.89E <sup>-09</sup>
IL21R	1.66218193	3.24E <sup>-06</sup>
ITGB2	1.660191473	6.22E <sup>-10</sup>
IL2RA	1.659106244	1.19E <sup>-05</sup>
MRC1	1.651088087	1.01E <sup>-07</sup>
KLRK1	1.646248207	1.01E <sup>-07</sup>
CD247	1.63887623	2.31E <sup>-07</sup>
ITGAX	1.627537174	1.27E <sup>-06</sup>
C3AR1	1.620167907	1.01E <sup>-07</sup>
TNFRSF9	1.617281196	8.84E <sup>-06</sup>
CD4	1.610947153	7.85E <sup>-13</sup>
CLECTA	1.603891284	9.56E <sup>-08</sup>
CCR4	1.596704791	6.60E <sup>-05</sup>
TLR8	1.592851237	2.71E <sup>-08</sup>
CD209	1.580960996	1.12E <sup>-05</sup>
BST2	1.576819838	2.05E <sup>-07</sup>
IL7R	1.565475358	4.23E <sup>-05</sup>
IFIT2	1.564689645	4.48E <sup>-05</sup>
HLA-DMB	1.564191477	1.96E <sup>-08</sup>
TIGIT	1.563162051	3.64E <sup>-06</sup>
FUT7	1.557799451	3.42E <sup>-05</sup>
LILRB1	1.553953951	5.86E <sup>-05</sup>
MARCO	1.553703623	5.31E <sup>-04</sup>
OAS3	1.546994494	8.30E <sup>-06</sup>
HLA-DQB1	1.542804204	1.76E <sup>-02</sup>
C2	1.542693492	4.30E <sup>-06</sup>
IFI27	1.525854402	6.88E <sup>-05</sup>
SIGLEC1	1.523424602	1.24E <sup>-05</sup>
CD1B	1.522087168	5.4E <sup>-03</sup>
CD3E	1.514546888	1.00E <sup>-06</sup>
SELL	1.496460311	2.22E <sup>-05</sup>
LY9	1.492315019	1.53E <sup>-07</sup>
CCR2	1.488987159	1.94E <sup>-06</sup>
TARP	1.483563718	1.69E <sup>-05</sup>
CTSW	1.482246845	7.47E <sup>-06</sup>
F13A1	1.472671683	9.84E <sup>-07</sup>
CD96	1.471749044	4.35E <sup>-07</sup>
CCL13	1.464536682	7.67E <sup>-04</sup>
MX1	1.46074994	0.000953455
CCL19	1.458698343	0.000602318
ITGAL	1.450189741	2.51E <sup>-05</sup>
CD38	1.449036275	0.00027041
FCGR2B	1.443028258	1.42E <sup>-10</sup>
LY96	1.440162539	3.23E <sup>-08</sup>
CFB	1.436060987	4.58E <sup>-06</sup>
IFITM1	1.433847803	1.27E <sup>-06</sup>
HAVCR2	1.429854578	3.16E <sup>-10</sup>
ICOS	1.424698348	0.000513781
LCK	1.423323638	7.89E <sup>-08</sup>
CD28	1.422732251	1.01E <sup>-05</sup>
GZMH	1.42243173	2.22E <sup>-05</sup>
CCL3L1	1.418558965	0.004708418
LTF	1.41457572	0.005932137
IL10RA	1.408137054	1.01E <sup>-11</sup>
CCR7	1.407974758	0.00196475
VCAM1	1.400957189	6.67E <sup>-07</sup>
FOXP3	1.386625115	0.000365591
CD68	1.38359601	4.72E <sup>-07</sup>
CD5	1.383126435	1.27E <sup>-06</sup>
KLRC2	1.382087803	0.000825181

HLA-G	1.378184589	7.47E <sup>-06</sup>
CD74	1.369125345	2.84E <sup>-06</sup>
SELE	1.358885964	0.00316245
CX3CR1	1.348772914	1.75E <sup>-05</sup>
PDCD1	1.342678056	0.000779329
CD79A	1.339049379	0.00295576
IRF1	1.32916762	1.75E <sup>-05</sup>
INPP5D	1.326791502	1.42E <sup>-10</sup>
C3	1.319632594	2.61E <sup>-05</sup>
HLA-DMA	1.312347193	3.88E <sup>-06</sup>
CHIT1	1.307736078	0.022457808
LILRA4	1.307366465	0.008905254
CD86	1.306149567	0.0002268
MSR1	1.295051071	1.19E <sup>-05</sup>
IL12RB1	1.28710024	0.000325291
IRF7	1.279719469	0.0002268
PDCD1LG2	1.27704318	3.65E <sup>-06</sup>
CXCL1	1.271792987	0.00884873
SOCS1	1.263138008	5.02E <sup>-05</sup>
CD274	1.257136507	0.000786564
PIK3CG	1.252822308	3.71E <sup>-06</sup>
BTLA	1.241711508	0.000868284
LAIR2	1.241691117	0.000872268
AMICA1	1.237415871	8.14E <sup>-07</sup>
CSF2	1.235232215	0.012196226
TNFSF14	1.233606776	5.77E <sup>-05</sup>
LTA	1.229292537	0.001841094
JAK3	1.219381406	0.000584673
ITGA4	1.202602679	1.86E <sup>-05</sup>
ICAM1	1.196994857	8.93E <sup>-06</sup>
CD84	1.19436403	1.00E <sup>-08</sup>
CD6	1.178264638	0.000308299
CMKLR1	1.176747021	1.63E <sup>-06</sup>
LILRB3	1.175980408	0.00249483
CD180	1.174706382	0.005932137
HLA-DRB3	1.17242994	0.001982257
ITK	1.1723483	0.000500812
CD1E	1.168435387	0.017040854
TNF	1.166604013	0.000584673
HCK	1.161271846	2.68E <sup>-05</sup>
CCL8	1.158072287	0.005584385
CD37	1.157267712	0.00295576
ITGAM	1.152076995	2.05E <sup>-06</sup>
MICB	1.150563386	1.19E <sup>-05</sup>
CFP	1.144262312	6.51E <sup>-05</sup>
STAT4	1.144100101	0.000333008
KIR2DL3	1.143001731	0.006297416
CD97	1.142879019	1.96E <sup>-08</sup>
TAP1	1.142052487	4.94E <sup>-06</sup>
PSMB10	1.140090572	1.19E <sup>-05</sup>
IFIT1	1.132404496	0.007676868
MEFV	1.131552017	0.003799779
CSF3R	1.130203545	6.02E <sup>-05</sup>
ZAP70	1.126096852	0.000175359
PSMB9	1.118659707	4.48E <sup>-05</sup>
TNFRSF1B	1.118003216	2.69E <sup>-07</sup>
SPN	1.110504202	0.000580813
KLRD1	1.10995538	0.001220199
SLC11A1	1.109150197	0.003515892
CLEC5A	1.104395359	0.000756391
CD40	1.103274453	4.80E <sup>-07</sup>
GZMM	1.102053892	0.003994252
IFIH1	1.096466865	0.000108958
HLA-B	1.093918753	5.47E <sup>-07</sup>
CD1C	1.093425001	0.01278048
XCR1	1.092025771	0.000858944

<i>BTK</i>	1.088264529	1.08E <sup>-05</sup>
<i>CXCL2</i>	1.086420393	0.040542955
<i>ISG20</i>	1.084887314	0.001771997
<i>IL2RB</i>	1.076363405	0.000175639
<i>CD8B</i>	1.076170759	0.001346439
<i>CD14</i>	1.068924112	0.001763805
<i>NCF4</i>	1.062393035	6.02E <sup>-05</sup>
<i>CCL22</i>	1.060626053	0.022042894
<i>CXCL3</i>	1.058356047	0.034564049
<i>KIR3DL2</i>	1.054927913	0.046551827
<i>TNFRSF11B</i>	1.054912213	0.011076697
<i>TAP2</i>	1.041351946	5.61E <sup>-05</sup>
<i>LYN</i>	1.041200598	0.00013837
<i>PIK3CD</i>	1.039168077	1.31E <sup>-05</sup>
<i>CD33</i>	1.036837165	0.000108958
<i>IRF4</i>	1.034578728	0.001441221
<i>TNFRSF17</i>	1.025477513	0.042732214
<i>HLA-C</i>	1.014680298	2.68E <sup>-05</sup>
<i>KLRB1</i>	1.01282837	0.00128477
<i>PSMB8</i>	1.007799043	1.43E <sup>-06</sup>
<i>TNFSF13</i>	1.007161918	6.26E <sup>-03</sup>

#### Supplementary Table 4. Ingenuity canonical pathways.

Top 25 Ingenuity canonical pathways overrepresented by the 202 differentially expressed genes in Grade 3 biopsies (n = 11), compared to Grade 0 (n = 10).

Ingenuity Canonical Pathways	$-\log(p\text{-value})^A$	DEG/Genes Ratio <sup>B</sup>
iCOS-iCOSL Signalling in T Helper Cells	5.79	0.587
Th1 Pathway	5.6	0.5
Allograft Rejection Signalling	5.59	0.667
CTLA4 Signalling in Cytotoxic T Lymphocytes	5.36	0.708
Antigen Presentation Pathway	5.36	0.708
Calcium-induced T Lymphocyte Apoptosis	5.26	0.75
Nur77 Signalling in T Lymphocytes	5.26	0.75
Th1 and Th2 Activation Pathway	4.98	0.45
B Cell Development	4.78	0.737
Autoimmune Thyroid Disease Signalling	4.54	0.667
Th2 Pathway	4.31	0.467
Cdc42 Signalling	4.26	0.594
Graft-versus-Host Disease Signalling	3.91	0.615
Pathogenesis of Multiple Sclerosis	3.85	0.889
Primary Immunodeficiency Signalling	3.63	0.593
OX40 Signalling Pathway	3.54	0.543
Role of NFAT in Regulation of the Immune Response	3.37	0.466
CD28 Signalling in T Helper Cells	2.83	0.46
Crosstalk between Dendritic Cells and Natural Killer Cells	2.54	0.431
T Helper Cell Differentiation	2.42	0.429
Super pathway of Inositol phosphate compounds	2.38	0.588
Communication between Innate and adaptive immune cells	2.3	0.417
Natural killer cell signalling	2.21	0.471
Type I diabetes mellitus signalling	2.09	0.4
Cytotoxic T lymphocyte-mediated apoptosis of target cells	2.01	0.562

<sup>A</sup>Benjamini-Hochberg corrected Fischer's exact test p values are shown.

<sup>B</sup>Ratio of the differentially expressed genes (DEG) that mapped to the pathway divided by the total number of genes that mapped to the canonical pathway.

**Supplementary Table 5. Gene ontology biological process terms.**

Top 20 Gene Ontology (GO) biological process terms enriched among the 202 differentially expressed genes in Grade 3 biopsies (n = 11), compared to Grade 0 (n = 10). Fisher's one-tailed test was used and p values were adjusted using Benjamini-Hochberg False Discovery Rate for multiple testing correction.

GO Biological Processes	GO ID	Benjamini's adjusted p-value
Lymphocyte co-stimulation	GO:0031294	2.26E <sup>-05</sup>
T cell co-stimulation	GO:0031295	2.26E <sup>-05</sup>
Immune system process	GO:0022376	2.75E <sup>-05</sup>
Leukocyte activation	GO:0045321	2.75E <sup>-05</sup>
Antigen processing and presentation of exogenous antigen	GO:0019884	6.02E <sup>-05</sup>
Antigen processing and presentation	GO:0019882	9.42E <sup>-05</sup>
T cell activation	GO:0042110	9.42E <sup>-05</sup>
Antigen processing and presentation of peptide antigen	GO:0048002	1.21E <sup>-04</sup>
Cell activation	GO:0001775	1.31E <sup>-04</sup>
Antigen processing and presentation of exogenous peptide antigen	GO:0002478	1.48E <sup>-04</sup>
Immune response	GO:0006955	1.48E <sup>-04</sup>
Lymphocyte activation	GO:0046649	1.50E <sup>-04</sup>
Antigen processing and presentation of exogenous peptide antigen via MHC class II	GO:0019886	1.56E <sup>-04</sup>
Leukocyte cell-cell adhesion	GO:0007159	1.51E <sup>-03</sup>
Antigen processing and presentation of peptide antigen via MHC class II	GO:0002495	1.84E <sup>-03</sup>
Antigen processing and presentation of peptide or polysaccharide antigen via MHC class II	GO:0002504	4.73E <sup>-03</sup>
Regulation of lymphocyte activation	GO:0051249	5.03E <sup>-03</sup>
Regulation of immune system process	GO:0002682	6.94E <sup>-03</sup>
Regulation of T cell activation	GO:0050863	8.42E <sup>-03</sup>
Positive regulation of lymphocyte activation	GO:0051251	8.68E <sup>-03</sup>

### Supplementary Table 6. Upstream regulators.

The upstream regulators of the 202 differentially expressed genes in Grade 3 biopsies (n = 11), compared to Grade 0 (n = 10).

Cytokine Upstream Regulator	Z-score <sup>A</sup>	P-value of overlap <sup>B</sup>
IFN $\gamma$	8.416	4.82E <sup>-06</sup>
TNF	7.701	3.43E <sup>-03</sup>
IL2	6.52	3.53E <sup>-05</sup>
CSF2	6.494	7.48E <sup>-03</sup>
IL18	4.815	1.95E <sup>-03</sup>

<sup>A</sup>Z-score accounts for both the total number of genes differentially expressed and direction of activation; a z-score  $\geq 2$  (activated) or  $\leq -2$  (inhibited) was considered significant.

<sup>B</sup>P-value of overlap represents the significance in the overlap between the identified differentially expressed genes (the known downstream targets) and all genes associated with a particular upstream regulator in the Ingenuity database.



**Supplementary Table 7. List of the 153 differentially expressed genes in Grade 2 biopsies compared to Grade 0.**

Differentially expressed genes (log2 fold change > 1; adjusted p value < 0.05) in Grade 2 biopsies (n = 8) compared to Grade 0 biopsies (n = 10) were evaluated using normalized gene expression counts as input and the Wald significance test. P values were adjusted using Benjamini-Hochberg procedure.

Gene Symbol	Log2 Fold Change	Adjusted p value
FOS	2.455652707	7.71E <sup>-04</sup>
CXCL9	2.209491481	7.71E <sup>-04</sup>
CT45A1	2.157359485	1.63E <sup>-03</sup>
CXCL2	2.102018385	6.36E <sup>-04</sup>
GZMB	1.90580579	6.36E <sup>-04</sup>
MARCO	1.884154274	6.36E <sup>-04</sup>
CXCL3	1.812645106	1.45E <sup>-03</sup>
LILRB3	1.811202713	1.84E <sup>-04</sup>
IFNB1	1.785339862	5.98E <sup>-03</sup>
ICAM4	1.766102906	2.37E <sup>-03</sup>
C1QB	1.718422306	2.35E <sup>-03</sup>
CD79A	1.710451026	1.48E <sup>-03</sup>
LAIR2	1.681420935	3.94E <sup>-04</sup>
GAGE1	1.664517231	1.04E <sup>-02</sup>
IL1RAPL2	1.66321669	1.50E <sup>-03</sup>
FCGR3A	1.66057526	6.18E <sup>-04</sup>
MS4A1	1.649967192	1.04E <sup>-02</sup>
CD22	1.631539768	2.03E <sup>-03</sup>
CD80	1.626937579	5.61E <sup>-03</sup>
POU2AF1	1.626183328	5.66E <sup>-03</sup>
CXCL10	1.621822078	1.39E <sup>-02</sup>
LILRB1	1.620578114	7.71E <sup>-04</sup>
CCL18	1.605107499	1.49E <sup>-02</sup>
TNFRSF17	1.601512981	4.17E <sup>-03</sup>
IL17F	1.598183772	1.23E <sup>-02</sup>
SSX1	1.591600596	1.02E <sup>-02</sup>
CXCL1	1.591064335	4.3E <sup>-03</sup>
MAGEC1	1.590939324	8.79E <sup>-03</sup>
CD180	1.563168965	1.91E <sup>-03</sup>
KIR3DL2	1.560513282	6.59E <sup>-03</sup>
SPO11	1.558902886	1.02E <sup>-02</sup>
ULBP2	1.558023389	4.66E <sup>-03</sup>
CXCL5	1.545228313	6.57E <sup>-03</sup>
CR1	1.542697541	2.37E <sup>-03</sup>
IL2RA	1.532446671	1.12E <sup>-03</sup>
IL5	1.529129187	1.58E <sup>-02</sup>
CYBB	1.526998136	1.84E <sup>-04</sup>
LILRA4	1.526535338	6.9E <sup>-03</sup>
CD19	1.500245448	2.37E <sup>-03</sup>
CCR1	1.496546371	8.89E <sup>-04</sup>
IFNA1	1.491409698	2.72E <sup>-02</sup>
CLEC4C	1.490920047	8.2E <sup>-03</sup>
PRM1	1.489332107	1.43E <sup>-02</sup>
CEACAM6	1.488984116	8.49E <sup>-03</sup>
FUT5	1.477350316	1.56E <sup>-02</sup>

IL27	1.473025646	1.24E <sup>-02</sup>
CD8A	1.468830529	6.36E <sup>-04</sup>
LILRA5	1.466766573	5.88E <sup>-03</sup>
CD163	1.466725971	2.32E <sup>-03</sup>
CCR9	1.465666559	2.55E <sup>-02</sup>
TNFSF18	1.460105613	1.98E <sup>-02</sup>
KLRC2	1.438121863	3.3E <sup>-03</sup>
MEFV	1.431754279	1.91E <sup>-03</sup>
IFNA7	1.423307163	2.46E <sup>-02</sup>
IDO1	1.406481241	3.6E <sup>-03</sup>
CD209	1.403930476	1.58E <sup>-03</sup>
CCR3	1.403135774	2.24E <sup>-02</sup>
LTB	1.401097331	1E <sup>-02</sup>
TNFRSF11B	1.399140579	3.36E <sup>-03</sup>
SSX4	1.394206267	3.1E <sup>-02</sup>
CSF3	1.388628186	1.04E <sup>-02</sup>
CD38	1.388360374	3.39E <sup>-03</sup>
FCER1G	1.385139695	1.84E <sup>-04</sup>
C9	1.382969686	1.5E <sup>-02</sup>
TLR8	1.382075206	1.84E <sup>-04</sup>
C3AR1	1.380628137	4.49E <sup>-04</sup>
CXCR3	1.379340333	1.63E <sup>-03</sup>
IL12RB1	1.367922752	1.63E <sup>-03</sup>
CCL15	1.363102103	2.81E <sup>-02</sup>
SLC11A1	1.359217792	2.37E <sup>-03</sup>
CCL19	1.354572483	6.59E <sup>-03</sup>
CCL4	1.34801205	3.38E <sup>-03</sup>
SELL	1.346057762	1.91E <sup>-03</sup>
MAGEA12	1.345155145	2.83E <sup>-02</sup>
CCL26	1.334470142	1.39E <sup>-02</sup>
CASP10	1.321114673	1.29E <sup>-02</sup>
SIGLEC1	1.320849018	2.03E <sup>-03</sup>
CCL1	1.320438647	3.55E <sup>-02</sup>
IL2	1.317105257	3.31E <sup>-02</sup>
C1QA	1.316340113	2.32E <sup>-03</sup>
CCR5	1.304702801	5.88E <sup>-03</sup>
CXCR1	1.300698461	2.25E <sup>-02</sup>
CR2	1.299775085	1.48E <sup>-02</sup>
MAGEA1	1.298780615	3.55E <sup>-02</sup>
IFNL2	1.298016765	3.59E <sup>-02</sup>
LY86	1.29698285	3.94E <sup>-04</sup>
CCR7	1.295105034	1.39E <sup>-02</sup>
CXCL11	1.290066485	1.95E <sup>-02</sup>
FCGR1A	1.280094986	8.2E <sup>-03</sup>
IL21R	1.279215804	3.3E <sup>-03</sup>
PAX5	1.271600078	1.35E <sup>-02</sup>
PDCD1	1.26752442	6.7E <sup>-03</sup>
XCL2	1.267522086	5.12E <sup>-03</sup>
CLEC7A	1.261274383	8.28E <sup>-04</sup>
STAT4	1.24688113	1.45E <sup>-03</sup>
ITGAX	1.24657862	2.37E <sup>-03</sup>
C2	1.243272902	2.37E <sup>-03</sup>
IFNA2	1.242444272	2.96E <sup>-02</sup>
FPR2	1.231563626	1.95E <sup>-02</sup>
FUT7	1.218619614	6.59E <sup>-03</sup>
CCR4	1.218142222	1.09E <sup>-02</sup>
FCGR2A	1.209587947	6.36E <sup>-04</sup>
CD2	1.208090111	3.95E <sup>-03</sup>
ISG15	1.204792378	1.95E <sup>-02</sup>
IL7R	1.195957062	8.81E <sup>-03</sup>
AMBP	1.191951549	2.7E <sup>-02</sup>
LILRB2	1.188870695	2.37E <sup>-03</sup>
TNFSF13	1.182566855	5.67E <sup>-03</sup>
CD28	1.17434713	2.76E <sup>-03</sup>
ATG12	1.167495823	1.24E <sup>-02</sup>

CD8B	1.167180913	3.37E <sup>-03</sup>
KLRF1	1.162898923	1.59E <sup>-02</sup>
CD48	1.160687732	3.16E <sup>-03</sup>
CD68	1.150476142	8.27E <sup>-04</sup>
CXCR6	1.143874367	6.57E <sup>-03</sup>
LAG3	1.14311045	6.44E <sup>-03</sup>
CCL3	1.139613232	3.09E <sup>-02</sup>
KLRC1	1.136957846	7.68E <sup>-03</sup>
BLK	1.13400885	2.49E <sup>-02</sup>
CD53	1.130768599	8.28E <sup>-04</sup>
CD37	1.128433334	1.24E <sup>-02</sup>
LTA	1.12791676	1.39E <sup>-02</sup>
MSR1	1.127121404	2.02E <sup>-03</sup>
CTSW	1.123315139	5.12E <sup>-03</sup>
MRC1	1.120686873	3.16E <sup>-03</sup>
THY1	1.116328967	1.58E <sup>-02</sup>
HLA-DRB3	1.107855802	1.24E <sup>-02</sup>
CTSS	1.104773928	1.22E <sup>-03</sup>
GZMK	1.104413632	6.84E <sup>-03</sup>
CD27	1.103585969	5.67E <sup>-03</sup>
CD3D	1.097111551	3.37E <sup>-03</sup>
IRF8	1.096880792	5.39E <sup>-03</sup>
TLR10	1.095212797	1.52E <sup>-02</sup>
ICAM1	1.09516621	1.12E <sup>-03</sup>
CMKLR1	1.085314698	6.36E <sup>-04</sup>
BTLA	1.070875022	1.45E <sup>-02</sup>
TARP	1.062855629	1.04E <sup>-02</sup>
TNFSF13B	1.059087445	5.95E <sup>-03</sup>
HLA-DOB	1.056175854	5.28E <sup>-03</sup>
CD79B	1.053888767	3.33E <sup>-02</sup>
ITGB2	1.052404892	1.63E <sup>-03</sup>
C4B	1.048068078	1.5E <sup>-02</sup>
PRF1	1.04770254	5.22E <sup>-03</sup>
ITGAL	1.044826263	1.15E <sup>-02</sup>
F13A1	1.038407237	4.53E <sup>-03</sup>
KIR2DL3	1.033529359	3.09E <sup>-02</sup>
CFB	1.024228759	6.59E <sup>-03</sup>
HLA-DMA	1.022231016	3.3E <sup>-03</sup>
SH2D1A	1.015544078	5.67E <sup>-03</sup>
JAK3	1.015065255	1.49E <sup>-02</sup>
CCL23	1.009173348	3.44E <sup>-02</sup>
SLAMF6	1.008554831	2.26E <sup>-02</sup>
FOXJ1	-1.915769459	4.3E <sup>-03</sup>

## Supplementary Table 8. Pattern analysis.

The list of 273 genes that progressively over-expressed as the rejection severity increased from Grade 0 through Grade 3 acute cellular rejection according to the pattern analysis. The pattern analysis is detailed in Methods.

Gene Symbol				
A2M	CD68	GZMH	ISG20	PTGS2
ADA	CD7	GZMK	ITGA4	PTPRC
AMICA1	CD74	GZMM	ITGA5	RELB
ANXA1	CD80	HAVCR2	ITGAL	RUNX3
BAX	CD83	HCK	ITGAM	S100B
BCL10	CD84	HLA-A	ITGAX	SBNO2
BST2	CD86	HLA-B	ITGB2	SELE
BTK	CD8A	HLA-C	ITK	SELL
BTLA	CD8B	HLA-DMA	JAK2	SELPLG
C1QA	CD96	HLA-DMB	JAK3	SERPING1
C1QB	CD97	HLA-DOB	KIR3DL3	SH2D1A
C1R	CFB	HLA-DPA1	KIR2DL3	SIGIRR
C1S	CFP	HLA-DPB1	KLRB1	SIGLEC1
C2	CHIT1	HLA-DQB1	KLRC2	SOCS1
C3	CKLF	HLA-DRA	KLRD1	SPN
C3AR1	CLEC4C	HLA-DRB3	KLRK1	SPP1
CARD11	CLEC7A	HLA-E	LAG3	ST6GAL1
CASP1	CMA1	HLA-G	LAMP3	STAT1
CASP3	CMKLR1	ICAM1	LCK	STAT2
CASP8	CR1	ICAM2	LCP1	STAT4
CCL13	CSF1R	ICAM3	LILRA4	SYK
CCL18	CSF2RB	ICOS	LRP1	TAP1
CCL19	CSF3R	IDO1	LTA	TAP2
CCL2	CTLA4	IFI16	LTB	TAPBP
CCL22	CTSL	IFI27	LY86	TARP
CCL4	CTSS	IFI35	LY9	TICAM2
CCL5	CTSW	IFIH1	LY96	TIGIT
CCL8	CX3CR1	IFIT1	LYN	TLR1
CCR1	CXCL10	IFIT2	MAP2K1	TLR2
CCR2	CXCL11	IFITM1	MFGE8	TLR3
CCR4	CXCL16	IFITM2	MICB	TLR7
CCR5	CXCL9	IFNGR1	MR1	TLR8
CCR7	CXCR3	IL10RA	MRC1	TNF
CD14	CXCR4	IL12RB1	MSR1	TNFAIP3
CD163	CXCR6	IL12RB2	MX1	TNFRSF14
CD2	CYBB	IL15	MYD88	TNFRSF1B
CD209	CYFIP2	IL15RA	NCF4	TNFRSF4
CD244	CYLD	IL17RA	NCR1	TNFRSF9
CD247	DDX58	IL1RL1	NFATC3	TNFSF13
CD27	ELK1	IL21R	NLRC5	TNFSF13B
CD274	ENG	IL2RA	OAS3	TNFSF14
CD28	ETS1	IL2RB	PDCD1	TNFSF4
CD33	F13A1	IL2RG	PDCD1LG2	TRAF2
CD37	FCER1G	IL3RA	PDGFC	TYK2
CD38	FCER2	IL6R	PECAM1	VCAM1
CD3D	FCGR2A	IL6ST	PIK3CD	XCL2
CD3E	FCGR2B	IL7R	PIK3CG	XCR1
CD3G	FCGR3A	INPP5D	PIN1	YTHDF2
CD4	FLT3	IRAK1	PLAU	ZAP70
CD40	FLT3LG	IRF1	ISG21	CNOT10
CD40LG	FOXP3	IRF2	ITGA6	NUBP1

<i>CD48</i>	<i>FUT7</i>	<i>IRF4</i>	<i>ITGA7</i>	<i>TMUB2</i>
<i>CD5</i>	<i>GNLY</i>	<i>IRF7</i>	<i>ITGAL</i>	<i>USP39</i>
<i>CD53</i>	<i>GZMA</i>	<i>IRF8</i>	<i>ITGAM</i>	
<i>CD6</i>	<i>GZMB</i>	<i>ISG15</i>	<i>ITGAX</i>	

### Supplementary Table 9. Top 20 Gene Ontology (GO) biological process terms.

Top 20 Gene Ontology (GO) biological process terms enriched among the 273 genes that progressively over-expressed as the rejection severity increased from Grade 0 through Grade 3 acute cellular rejection. The complete list of 273 genes is shown in Supplementary Table 8. P values were obtained using Fisher's one-tailed test and adjusted using Benjamini-Hochberg False Discovery Rate for multiple testing correction.

GO Biological Processes	GO ID	Benjamini's adjusted p-value
T cell costimulation	GO:0031295	2.69E <sup>-06</sup>
Lymphocyte costimulation	GO:0031294	1.73E <sup>-05</sup>
Immune system process	GO:0002376	5.59E <sup>-04</sup>
Positive regulation of leukocyte cell-cell adhesion	GO:1903039	6.43E <sup>-04</sup>
Leukocyte cell-cell adhesion	GO:0007159	1.63E <sup>-03</sup>
Positive regulation of T cell activation	GO:0050870	1.95E <sup>-03</sup>
Positive regulation of cell-cell adhesion	GO:0022409	2.55E <sup>-03</sup>
Regulation of leukocyte cell-cell adhesion	GO:1903037	5.42E <sup>-03</sup>
Regulation of T cell activation	GO:0050863	6.15E <sup>-03</sup>
Antigen processing and presentation of exogenous peptide antigen	GO:0002478	6.15E <sup>-03</sup>
Antigen processing and presentation of peptide antigen	GO:0048002	6.37E <sup>-03</sup>
Immune response	GO:0006955	9.07E <sup>-03</sup>
Positive regulation of lymphocyte activation	GO:0051251	9.07E <sup>-03</sup>
T cell activation	GO:0042110	1.58E <sup>-02</sup>
Positive regulation of cell activation	GO:0050867	1.58E <sup>-02</sup>
Positive regulation of leukocyte activation	GO:0002696	1.66E <sup>-02</sup>
Cellular response to type I interferon	GO:0071357	1.67E <sup>-02</sup>
Type I interferon signalling pathway	GO:0060337	1.67E <sup>-02</sup>
Cell-cell adhesion	GO:0098609	2.13E <sup>-02</sup>
Regulation of lymphocyte activation	GO:0051249	2.13E <sup>-02</sup>

**Supplementary Table 10. List of 107 genes that were exclusively differentially expressed in Grade 3 biopsies.**

List of 107 genes that were exclusively differentially expressed in Grade 3 biopsies (n = 11) but not in Grade 2 (n = 8), when compared to Grade 0 (n = 10).

<b>Gene Symbol</b>				
<i>AMICA1</i>	<i>CD6</i>	<i>HLA-B</i>	<i>ISG20</i>	<i>PSMB8</i>
<i>BST2</i>	<i>CD74</i>	<i>HLA-C</i>	<i>ITGA4</i>	<i>PSMB9</i>
<i>BTK</i>	<i>CD83</i>	<i>HLA-DMB</i>	<i>ITGAM</i>	<i>PTPRC</i>
<i>C3</i>	<i>CD84</i>	<i>HLA-DPA1</i>	<i>ITK</i>	<i>SELE</i>
<i>CCL13</i>	<i>CD86</i>	<i>HLA-DPB1</i>	<i>KLRB1</i>	<i>SELPLG</i>
<i>CCL22</i>	<i>CD96</i>	<i>HLA-DQA1</i>	<i>KLRD1</i>	<i>SOCS1</i>
<i>CCL3L1</i>	<i>CD97</i>	<i>HLA-DQB1</i>	<i>KLRK1</i>	<i>SPN</i>
<i>CCL5</i>	<i>CFP</i>	<i>HLA-DRA</i>	<i>LAMP3</i>	<i>STAT1</i>
<i>CCL8</i>	<i>CHIT1</i>	<i>HLA-G</i>	<i>LCK</i>	<i>TAP1</i>
<i>CCR2</i>	<i>CLEC5A</i>	<i>ICOS</i>	<i>LCP1</i>	<i>TAP2</i>
<i>CD14</i>	<i>CSF2</i>	<i>IFI27</i>	<i>LTF</i>	<i>TIGIT</i>
<i>CD1B</i>	<i>CSF3R</i>	<i>IFIH1</i>	<i>LY9</i>	<i>TNF</i>
<i>CD1C</i>	<i>CTLA4</i>	<i>IFIT1</i>	<i>LY96</i>	<i>TNFRSF1B</i>
<i>CD1E</i>	<i>CX3CR1</i>	<i>IFIT2</i>	<i>LYN</i>	<i>TNFRSF4</i>
<i>CD247</i>	<i>FCGR2B</i>	<i>IFITM1</i>	<i>MICB</i>	<i>TNFRSF9</i>
<i>CD274</i>	<i>FOXP3</i>	<i>IL10RA</i>	<i>MX1</i>	<i>TNFSF14</i>
<i>CD33</i>	<i>GNLY</i>	<i>IL2RB</i>	<i>NCF4</i>	<i>VCAM1</i>
<i>CD3E</i>	<i>GZMA</i>	<i>IL2RG</i>	<i>OAS3</i>	<i>XCR1</i>
<i>CD3G</i>	<i>GZMH</i>	<i>INPP5D</i>	<i>PDCD1LG2</i>	<i>ZAP70</i>
<i>CD4</i>	<i>GZMM</i>	<i>IRF1</i>	<i>PIK3CD</i>	
<i>CD40</i>	<i>HAVCR2</i>	<i>IRF4</i>	<i>PIK3CG</i>	
<i>CD5</i>	<i>HCK</i>	<i>IRF7</i>	<i>PSMB10</i>	

## Supplementary Table 11. Literature searches for the scoping review.

Details of the literature searches run and imported to Endnote for the scoping review.

Database	Search Terms	Results
<b>PubMed</b>	((("Gene Expression"[Mesh] OR (gene[tiab] AND expression[tiab]) OR biomarkers[MeSH] OR biomarker*[tiab] OR (overexpress*[tiab] AND gene*[tiab]) OR molecular marker*[tiab] OR gene*[tiab] OR signature gene*[tiab]) AND ("Organ Transplantation"[Mesh] OR organ transplant*[tiab] OR allotransplantation[tiab] OR allograft*[tiab] OR intragraft[tiab] OR "solid organ transplant"[tiab]) AND ("Graft Rejection"[Mesh])) AND (rejection[ti] OR (gene*[ti] AND expression[ti]) OR allo*[ti])) AND "Humans"[Mesh])	2340
<b>Web of Science</b> Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years	TS = ("gene expression" OR "biomarker" OR "molecular marker" OR "signature gene" OR "overexpression") AND TS = ("organ transplantation" OR "organ transplant" OR "allotransplantation" OR allograft* OR intragraft* OR "solid organ transplant") AND TS = ("Graft rejection" OR "rejection")	2526
<b>Embase</b>	('gene expression':ti,ab,kw OR 'biological marker':ti,ab,kw OR 'gene overexpression':ti,ab,kw OR 'molecular marker':ti,ab,kw OR 'signature gene':ti,ab,kw) AND ('organ transplantation':ti,ab,kw OR 'allograft':ti,ab,kw OR 'allotransplantation':ti,ab,kw OR 'intragraft':ti,ab,kw OR 'solid organ transplantation':ti,ab,kw OR 'solid organ transplant':ti,ab,kw) AND ('graft rejection':ti,ab,kw OR 'rejection':ti,ab,kw) AND 'human':ti,ab,kw	315
<b>Countway Discovery Medicine-EBSCO</b>	AB ( "gene expression" OR "biomarker" OR "molecular marker" OR "signature gene" OR "overexpression" ) AND AB ( "organ transplantation" OR "organ transplant" OR "allotransplantation" OR allograft* OR intragraft* OR "solid organ transplant" ) AND AB ( "Graft rejection" OR "rejection" )	1124



## Supplementary Table 12. Genes shared with solid organ transplant rejection.

166/202 genes upregulated in face transplant severe Grade 3 acute rejection (when compared to non-rejection biopsies) were shared with genes previously reported to be increased in solid organ transplants (kidney, liver, heart) during acute rejection. Details of the 202 differentially expressed genes are listed in Supplementary Table 3. P values were obtained using the Wald test and adjusted using Benjamini-Hochberg procedure.

Gene Symbol	Log2 fold change (Grade 0 vs. 3 in face transplants)	Adjusted p value (Grade 0 vs. 3 in face transplants)	Literature in Solid Organ Transplant Studies*
<i>GZMB</i>	3.408399293	2.44E <sup>-14</sup>	Kidney(2-11), Heart(12-15), Liver(16, 17)
<i>CXCL10</i>	3.254782936	7.73E <sup>-09</sup>	Kidney(10, 18, 19), Heart(15, 20), Liver(21)
<i>CXCL9</i>	3.018622816	1.54E <sup>-08</sup>	Kidney(10, 19), Kidney and Heart(22), Heart(15, 20), Liver(17, 21)
<i>CCL18</i>	2.492905496	1.02E <sup>-05</sup>	Kidney and Heart(22), Heart(14)
<i>IDO1</i>	2.345913685	4.38E <sup>-09</sup>	Kidney(19), Heart(15)
<i>C1QB</i>	2.28873685	8.12E <sup>-07</sup>	Kidney(23), Heart(15)
<i>CXCR3</i>	2.257045809	1.42E <sup>-10</sup>	Heart(20)
<i>LAG3</i>	2.229244219	1.24E <sup>-10</sup>	Kidney(24, 25), Heart(14)
<i>CXCL11</i>	2.039479683	1.21E <sup>-05</sup>	Kidney(10, 19), Heart(15, 20)
<i>IL2RG</i>	2.036657811	3.61E <sup>-11</sup>	Heart(15), Liver(26)
<i>XCL2</i>	2.027650828	5.73E <sup>-08</sup>	Kidney(10)
<i>FCGR3A</i>	2.024118189	6.86E <sup>-08</sup>	Kidney(23), Heart(15)
<i>ISG15</i>	2.022203685	2.99E <sup>-06</sup>	Heart(14)
<i>CLEC4C</i>	2.005658346	2.42E <sup>-05</sup>	Heart(14)
<i>IRF8</i>	1.995988235	7.12E <sup>-10</sup>	Heart(27)
<i>HLA-DRA</i>	1.969404649	2.23E <sup>-11</sup>	Kidney and Heart(22), Liver(17, 21)
<i>CD3D</i>	1.938555344	2.29E <sup>-10</sup>	Kidney(23, 25), Heart(15), Liver(17)
<i>CTSS</i>	1.894946302	4.84E <sup>-12</sup>	Kidney and Heart(22), Heart(15)
<i>LTB</i>	1.889930162	3.61E <sup>-05</sup>	Kidney and Heart(22), Heart(14), Liver(17)
<i>GZMK</i>	1.889537791	2.71E <sup>-08</sup>	Kidney and Heart(22), Heart(14)
<i>CD2</i>	1.885599484	4.01E <sup>-08</sup>	Kidney(23), Kidney and Heart(22), Heart(14), Liver(17, 21)
<i>CD8A</i>	1.884316831	2.71E <sup>-08</sup>	Kidney(10, 19, 23-25), Heart(14, 15), Liver(17)
<i>GNLY</i>	1.882614297	4.46E <sup>-05</sup>	Kidney(28)
<i>C1QA</i>	1.861448083	1.09E <sup>-07</sup>	Kidney and Heart(22)
<i>CD163</i>	1.857206159	2.17E <sup>-06</sup>	Kidney(23)
<i>CD53</i>	1.829408761	1.01E <sup>-11</sup>	Kidney(23), Kidney and Heart(22), Heart(15)
<i>PTPRC</i>	1.823290478	9.13E <sup>-13</sup>	Kidney and Heart(22), Heart(15)
<i>CCR1</i>	1.817694789	5.10E <sup>-07</sup>	Kidney(29, 30)
<i>CCL4</i>	1.799557075	2.11E <sup>-06</sup>	Kidney(10)
<i>HLA-DPB1</i>	1.794999976	3.70E <sup>-14</sup>	Kidney(10), Heart(14)
<i>SELPLG</i>	1.793854415	9.01E <sup>-16</sup>	Kidney and Heart(22)
<i>CTLA4</i>	1.78880823	5.18E <sup>-06</sup>	Kidney(3, 8, 25, 31), Heart(13)
<i>SH2D1A</i>	1.775909849	3.83E <sup>-09</sup>	Kidney(25)
<i>PRF1</i>	1.771469169	9.88E <sup>-09</sup>	Kidney(2-4, 7, 9-11, 19), Heart(12, 32)
<i>CD3G</i>	1.763318844	4.01E <sup>-08</sup>	Liver(17)
<i>GZMA</i>	1.750937452	2.09E <sup>-08</sup>	Kidney(10, 23), Heart(32, 33), Liver(26)
<i>HLA-DPA1</i>	1.749449127	1.01E <sup>-11</sup>	Kidney(10), Heart(14)
<i>CCL5</i>	1.742809019	4.08E <sup>-07</sup>	Kidney(10, 19, 23, 29, 34, 35), Kidney and Heart(22), Heart(15, 20)
<i>TNFSF13B</i>	1.722516488	6.33E <sup>-08</sup>	Kidney and Heart(22)
<i>CYBB</i>	1.717387747	3.12E <sup>-08</sup>	Kidney(23)
<i>LAMP3</i>	1.716565652	5.24E <sup>-06</sup>	Kidney(30), Heart(14)

CD27	1.71537078	1.86E <sup>-07</sup>	Kidney(23), Heart(14, 36), Liver(17)
STAT1	1.714005729	2.82E <sup>-07</sup>	Kidney and Heart(22), Heart(15)
FCGR2A	1.698741423	1.09E <sup>-09</sup>	Kidney(23)
LCP1	1.689301726	5.24E <sup>-11</sup>	Kidney(23), Kidney and Heart(22), Heart(14, 15)
CD80	1.686424973	0.000756391	Kidney(31), Heart(37)
CCR5	1.68192851	1.98E <sup>-05</sup>	Kidney(18), Heart(14, 20)
CD48	1.679219002	1.69E <sup>-07</sup>	Kidney(23), Liver(17)
CR1	1.675121323	6.60E <sup>-05</sup>	Kidney(25)
HLA-DQA1	1.673744106	0.013162812	Kidney and Heart(22), Heart(14)
CD83	1.670818169	4.77E <sup>-07</sup>	Liver(21)
CXCR6	1.668507932	1.75E <sup>-06</sup>	Kidney(25)
FCER1G	1.662460795	1.89E <sup>-09</sup>	Kidney(23), Kidney and Heart(22), Heart(15), Liver(17)
IL21R	1.66218193	3.24E <sup>-06</sup>	Kidney(24, 25), Heart(38), Liver(17)
ITGB2	1.660191473	6.22E <sup>-10</sup>	Kidney(23), Kidney and Heart(22), Heart(15, 27)
IL2RA	1.659106244	1.19E <sup>-05</sup>	Kidney(8)
MRC1	1.651088087	1.01E <sup>-07</sup>	Kidney(23)
KLRK1	1.646248207	1.01E <sup>-07</sup>	Kidney(10, 39)
CD247	1.63887623	2.31E <sup>-07</sup>	Kidney and Heart(22)
C3AR1	1.620167907	1.01E <sup>-07</sup>	Heart(15)
TNFRSF9	1.617281196	8.84E <sup>-06</sup>	Kidney(19)
CD4	1.610947153	7.85E <sup>-13</sup>	Heart(14)
CLECTA	1.603891284	9.56E <sup>-08</sup>	Kidney(19)
CCR4	1.596704791	6.60E <sup>-05</sup>	Kidney(23)
TLR8	1.592851237	2.71E <sup>-08</sup>	Kidney(40, 41)
CD209	1.580960996	1.12E <sup>-05</sup>	Kidney(30)
BST2	1.576819838	2.05E <sup>-07</sup>	Kidney and Heart(22)
IL7R	1.565475358	4.23E <sup>-05</sup>	Kidney(23)
HLA-DMB	1.564191477	1.96E <sup>-08</sup>	Kidney(19), Kidney and Heart(22)
TIGIT	1.563162051	3.64E <sup>-06</sup>	Kidney(19, 24, 25)
LILRB1	1.553953951	5.86E <sup>-05</sup>	Kidney(10)
MARCO	1.553703623	0.00053121	Kidney(42)
HLA-DQB1	1.542804204	0.017649896	Kidney(10), Kidney and Heart(22), Liver(21)
C2	1.542693492	4.30E <sup>-06</sup>	Kidney(41)
IFI27	1.525854402	6.88E <sup>-05</sup>	Heart(14)
SIGLEC1	1.523424602	1.24E <sup>-05</sup>	Kidney(43)
CD3E	1.514546888	1.00E <sup>-06</sup>	Kidney(23)
SELL	1.496460311	2.22E <sup>-05</sup>	Kidney and Heart(22), Liver(26)
CCR2	1.488987159	1.94E <sup>-06</sup>	Liver(17)
TARP	1.483563718	1.69E <sup>-05</sup>	Heart(44)
CD96	1.471749044	4.35E <sup>-07</sup>	Kidney(24, 25)
CCL13	1.464536682	0.000766965	Heart(14)
MX1	1.46074994	0.000953455	Kidney and Heart(22)
CCL19	1.458698343	0.000602318	Kidney(19), Kidney and Heart(22), Liver(17)
ITGAL	1.450189741	2.51E <sup>-05</sup>	Heart(44)
CD38	1.449036275	0.00027041	Heart(14), Liver(21)
FCGR2B	1.443028258	1.42E <sup>-10</sup>	Heart(14)
LY96	1.440162539	3.23E <sup>-08</sup>	Kidney(23), Kidney and Heart(22)
CFB	1.436060987	4.58E <sup>-06</sup>	Heart(45)
IFITM1	1.433847803	1.27E <sup>-06</sup>	Kidney(23)
HAVCR2	1.429854578	3.16E <sup>-10</sup>	Kidney(46)
ICOS	1.424698348	0.000513781	Kidney(25, 31)
LCK	1.423323638	7.89E <sup>-08</sup>	Kidney(23), Kidney and Heart(22), Liver(17)
CD28	1.422732251	1.01E <sup>-05</sup>	Kidney(24, 25, 31)
GZMH	1.42243173	2.22E <sup>-05</sup>	Heart(14)
LTF	1.41457572	0.005932137	Kidney(23)
IL10RA	1.408137054	1.01E <sup>-11</sup>	Heart(14)
CCR7	1.407974758	0.00196475	Heart(14)
VCAM1	1.400957189	6.67E <sup>-07</sup>	Heart(47), Liver(26)
FOXP3	1.386625115	0.000365591	Kidney(8, 9, 30, 48-50), Heart(51)
CD68	1.38359601	4.72E <sup>-07</sup>	Heart(15)
KLRC2	1.382087803	0.000825181	Heart(44)
HLA-G	1.378184589	7.47E <sup>-06</sup>	Kidney and Heart(22)
CD74	1.369125345	2.84E <sup>-06</sup>	Kidney and Heart(22), Heart(14, 15)

SELE	1.358885964	0.00316245	Liver(26)
CX3CR1	1.348772914	1.75E <sup>-05</sup>	Kidney(52)
PDCD1	1.342678056	0.000779329	Kidney(31)
IRF1	1.32916762	1.75E <sup>-05</sup>	Kidney(10, 19), Kidney and Heart(22)
INPP5D	1.326791502	1.42E <sup>-10</sup>	Kidney and Heart(22), Heart(14)
C3	1.319632594	2.61E <sup>-05</sup>	Kidney(30, 31, 53, 54), Heart(45)
HLA-DMA	1.312347193	3.88E <sup>-06</sup>	Kidney and Heart(22), Liver(21)
CHIT1	1.307736078	0.022457808	Kidney(42)
CD86	1.306149567	0.0002268	Kidney(25, 31), Heart(37)
IL12RB1	1.28710024	0.000325291	Kidney(24, 25)
IRF7	1.279719469	0.0002268	Kidney and Heart(22), Liver(55)
PDCD1LG2	1.27704318	3.65E <sup>-06</sup>	Kidney(25), Heart(44)
CXCL1	1.271792987	0.00884873	Kidney(56)
CD274	1.257136507	0.000786564	Kidney(25)
BTLA	1.241711508	0.000868284	Kidney(24, 25)
LAIR2	1.241691117	0.000872268	Heart(44)
AMICA1	1.237415871	8.14E <sup>-07</sup>	Liver(17)
CSF2	1.235232215	0.012196226	Kidney(30)
TNFSF14	1.233606776	5.77E <sup>-05</sup>	Heart(14)
LTA	1.229292537	0.001841094	Kidney(30)
JAK3	1.219381406	0.000584673	Kidney(43)
ITGA4	1.202602679	1.86E <sup>-05</sup>	Liver(26)
ICAM1	1.196994857	8.93E <sup>-06</sup>	Kidney(18), Heart(14, 47)
CD84	1.19436403	1.00E <sup>-08</sup>	Kidney(25)
CD6	1.178264638	0.000308299	Kidney and Heart(22), Heart(44)
LILRB3	1.175980408	0.00249483	Heart(14)
HLA-DRB3	1.17242994	0.001982257	Kidney and Heart(22)
ITK	1.1723483	0.000500812	Kidney(25), Heart(44)
TNF	1.166604013	0.000584673	Kidney(18, 57, 58), Heart(13)
HCK	1.161271846	2.68E <sup>-05</sup>	Kidney(43)
CCL8	1.158072287	0.005584385	Heart(27)
CD37	1.157267712	0.00295576	Kidney(23)
ITGAM	1.152076995	2.05E <sup>-06</sup>	Heart(14)
MICB	1.150563386	1.19E <sup>-05</sup>	Kidney(23)
CFP	1.144262312	6.51E <sup>-05</sup>	Kidney and Heart(22)
TAP1	1.142052487	4.94E <sup>-06</sup>	Kidney(10, 19, 25), Kidney and Heart(22), Heart(14, 15), Liver(21)
PSMB10	1.140090572	1.19E <sup>-05</sup>	Kidney and Heart(22), Heart(44)
ZAP70	1.126096852	0.000175359	Kidney and Heart(22), Heart(14)
PSMB9	1.118659707	4.48E <sup>-05</sup>	Kidney(10, 19), Kidney and Heart(22)
TNFRSF1B	1.118003216	2.69E <sup>-07</sup>	Kidney(23)
KLRD1	1.10995538	0.001220199	Kidney(10)
CLECSA	1.104395359	0.000756391	Kidney and Heart(22)
CD40	1.103274453	4.80E <sup>-07</sup>	Kidney(31), Heart(14, 37)
GZMM	1.102053892	0.003994252	Heart(14)
IFIH1	1.096466865	0.000108958	Heart(14)
HLA-B	1.093918753	5.47E <sup>-07</sup>	Kidney and Heart(22), Heart(14)
XCR1	1.092025771	0.000858944	Kidney and Heart(22)
CXCL2	1.086420393	0.040542955	Kidney(59)
ISG20	1.084887314	0.001771997	Kidney(10), Kidney and Heart(22)
IL2RB	1.076363405	0.000175639	Kidney and Heart(22), Heart(15), Liver(26)
CD8B	1.076170759	0.001346439	Kidney(25), Heart(14), Liver(17)
CD14	1.068924112	0.001763805	Kidney(23), Kidney and Heart(22), Heart(15)
NCF4	1.062393035	6.02E <sup>-05</sup>	Kidney(42)
CCL22	1.060626053	0.022042894	Kidney(60)
TAP2	1.041351946	5.61E <sup>-05</sup>	Kidney(10)
LYN	1.041200598	0.00013837	Heart(15)
PIK3CD	1.039168077	1.31E <sup>-05</sup>	Kidney and Heart(22)
CD33	1.036837165	0.000108958	Heart(14)
TNFRSF17	1.025477513	0.042732214	Kidney(42), Heart(14)
HLA-C	1.014680298	2.68E <sup>-05</sup>	Heart(14)
KLRB1	1.01282837	0.00128477	Kidney(43)
PSMB8	1.007799043	1.43E <sup>-06</sup>	Kidney(19), Heart(15)

\*For each gene, the table provides the literature references where the gene is shown to be upregulated in human solid organ transplant biopsies during acute rejection compared to the biopsies collected during non-rejection.

### Supplementary Table 13. Genes unique to face transplant rejection.

36/202 genes upregulated in face transplant severe Grade 3 rejection (n = 11) (compared to non-rejection biopsies, Grade 0; n=10) were unique to face transplant rejection. Details of the 202 differentially expressed genes are listed in Supplementary Table 3. P values were obtained using the Wald test and adjusted using Benjamini-Hochberg procedure.

Gene Symbol	Log2 fold change (Grade 0 vs. 3 in face transplants)	Adjusted p value (Grade 0 vs. 3 in face transplants)	Functional Annotation
<i>FUT7</i>	1.557799451	3.42E <sup>-05</sup>	Skin homing
<i>HLA-DOB</i>	1.752992601	1.96E <sup>-08</sup>	Immunoregulation
<i>LY9</i>	1.492315019	1.53E <sup>-07</sup>	Immunoregulation
<i>LILRA4</i>	1.307366465	8.9E <sup>-03</sup>	Immunoregulation
<i>MEFV</i>	1.131552017	3.8E <sup>-03</sup>	Immunoregulation
<i>SOCS1</i>	1.263138008	5.02E <sup>-05</sup>	Immunoregulation
<i>TNFRSF11B</i>	1.054912213	1.1E <sup>-02</sup>	Immunoregulation
<i>LY86</i>	1.728837002	7.25E <sup>-10</sup>	Immunoregulation
<i>CD180</i>	1.174706382	5.93E <sup>-03</sup>	Immunoregulation
<i>KIR3DL2</i>	1.054927913	4.66E <sup>-02</sup>	Immunoregulation
<i>KIR2DL3</i>	1.143001731	6.3E <sup>-03</sup>	Immunoregulation
<i>MSR1</i>	1.295051071	1.19E <sup>-05</sup>	APC and innate cell adhesion
<i>ITGAX</i>	1.627537174	1.27E <sup>-06</sup>	APC and innate cell adhesion
<i>CD97</i>	1.142879019	1.96E <sup>-08</sup>	APC and innate cell adhesion
<i>F13A1</i>	1.472671683	9.84E <sup>-07</sup>	APC and innate cell adhesion
<i>IRF4</i>	1.034578728	1.44E <sup>-03</sup>	Type I interferon signaling
<i>OAS3</i>	1.546994494	8.30E <sup>-06</sup>	Type I interferon signaling
<i>IFIT1</i>	1.132404496	7.68E <sup>-03</sup>	Type I interferon signaling
<i>IFIT2</i>	1.564689645	4.48E <sup>-05</sup>	Type I interferon signaling
<i>CD5</i>	1.383126435	1.27E <sup>-06</sup>	Co-stimulation
<i>TNFRSF4</i>	1.790937255	1.58E <sup>-06</sup>	Co-stimulation
<i>SPN</i>	1.110504202	5.8E <sup>-04</sup>	Co-stimulation
<i>CD1B</i>	1.522087168	5.4E <sup>-03</sup>	Lipid presentation
<i>CD1E</i>	1.168435387	1.7E <sup>-02</sup>	Lipid presentation
<i>CD1C</i>	1.093425001	1.28E <sup>-02</sup>	Lipid presentation
<i>CD79A</i>	1.339049379	2.96E <sup>-03</sup>	B cell related
<i>TNFSF13</i>	1.007161918	6.26E <sup>-03</sup>	B cell related
<i>BTK</i>	1.088264529	1.08E <sup>-05</sup>	B cell related
<i>CXCL3</i>	1.058356047	3.46E <sup>-02</sup>	Chemokines and receptors
<i>CCL3L1</i>	1.418558965	4.7E <sup>-03</sup>	Chemokines and receptors
<i>CMKLR1</i>	1.176747021	1.63E <sup>-06</sup>	Chemokines and receptors
<i>PIK3CG</i>	1.252822308	3.71E <sup>-06</sup>	Other
<i>CSF3R</i>	1.130203545	6.02E <sup>-05</sup>	Other
<i>SLC11A1</i>	1.109150197	3.51E <sup>-03</sup>	Other
<i>STAT4</i>	1.144100101	3.33E <sup>-04</sup>	Other
<i>CTSW</i>	1.482246845	7.47E <sup>-06</sup>	Other

**Supplementary Table 14. CDR3 sequences predicted to bind CD1b or CD1c by the GLIPH algorithm.**

CD1b-associated sequences		CD1c-associated sequences	
CASSRSSDRANNQPQHF	CASSVLDLSLHNEQFF	CASKRRGVRKTYGYTF	CASSLVPTGELFF
CASSQDNTGGASYEQYF	CASSRRSHFVLDEQYF	CASIRNLP GKTYGYTF	CASSLGGGPTGELFF
CASSFTSGRLLNTGELFF	CASSRK FVLDEQYF	CASGSTR AARLVGDSRKTYGYTF	CASSAPTGETQYF
CASRDGLAGGFKQETQYF	CASSQHCVLDEQYF	CASAPIYPRKTYGYTF	CASSPKTGRV IPEAFF
CSVSQGLAYKSRANVLTF	CASSQGPLNTGELFF	CSVSQGLAYKSRANVLTF	CASSAGSLPHQPQHF
CSASKITSGVQETQYF	CASSQGPFKAYNSPLHF	CSASKITSGVQETQYF	CSAREHTGHQPQHF
CSARLLEREQFF	CASSQESASGNLNTGELFF	CSARLLEREQFF	CASSSAGHQ PQHF
CSARLLDFEAF	CASSQDRLLAQHSPLHF	CSARLLDFEAF	CASSQERKETYEQYF
CGRQRKITQSRANVLTF	CASSFVLDEQYF	CGRQRKITQSRANVLTF	CASSQSRGWADTQYF
CAWSVLDREAEQYF	CASRN RVLHVLDEQYF	CAWSVLDREAEQYF	CASRTIARKRYEQYF
CATSRKGYNSPLHF	CASIKGGLNTGELFF	CAVRNTGGFKTIF	CASKSRLENTEAFF
CASSYRFIPYYGYTF	CASSSAGHQ PQHF	CATSRKGYNSPLHF	CTSSEHCLCTSRANVLTF
CASSVNVATVMQDTQYF	CASSQERKETYEQYF	CASSYRFIPYYGYTF	CTSR L C S C A Q S R A N V L T F
CASSVLDLSLHNEQFF	CASSQSRGWADTQYF	CASSVNVATVMQDTQYF	CTSRIRGLCTSRANVLTF
CASSVDLTRKTYGYTF	CASRTIARKRYEQYF	CASSVLDLSLHNEQFF	CSVQGGQLAYKGRANVLTF
CASSSKRSRKYTYGYTF	CASKSRLENTEAFF	CASSVDLTRKTYGYTF	CSAHHGGNTIYF
CASSSAGTGGFMNTEAFF	CTSSEHCLCTSRANVLTF	CASSSKRSRKYTYGYTF	CGNYFKITQSRANVLTF
CASSRYDSASQSRANVLTF	CTSRQVCLRKTYGYTF	CASSSAGTGGFMNTEAFF	CAWSLQCYRKTYGYTF
CASSRTGGGGYTF	CTSRLLRLWRKYTYGYTF	CASSRYDSASQSRANVLTF	CAWLSRVIQSRANVLTF
CASSRSRYHDKGRANVLTF	CTSR L C S C A Q S R A N V L T F	CASSRTGGGGYTF	CATSSNIGCGKTYGYTF
CASSRRSPFVMQDTQYF	CTSRIRGLCTSRANVLTF	CASSRSSDRANNQPQHF	CATSGRNSQSRANVLTF
CASSRRSHFVLDEQYF	CSVQGGQLAYKGRANVLTF	CASSRSRYHDKGRANVLTF	CASSYIIPICMQDTQYF
CASSRRLATWHHQ PQHF	CGSALRIRKTYGYTF	CASSRRSPFVMQDTQYF	CASSYFWHHQPQHF
CASSRRGPFVMQDTQYF	CGNYFKITQSRANVLTF	CASSRRSHFVLDEQYF	CASSVIMRKTYGYTF
CASSRQPICKRKNIQYF	CAWSLQCYRKTYGYTF	CASSRRGPFVMQDTQYF	CASSVGNPIFMQDTQYF
CASSRNPILQRKNIQYF	CAWLSRVIQSRANVLTF	CASSRQPICKRKNIQYF	CASSVDTGRKTQYF
CASSRK FVLDEQYF	CATSSNIGCGKTYGYTF	CASSRNPILQRKNIQYF	CASSVCAPFIHNSPLHF
CASSQKIATHARNTIYF	CATSGRNSQSRANVLTF	CASSRK FVLDEQYF	CASSTWVISQSRANVLTF
CASSQHCVLDEQYF	CATSDFRGYNEQFF	CASSQKIATHARNTIYF	CASSTPLPFVMQDTQYF
CASSQGPLNTGELFF	CATSDFLAGDTGELFF	CASSQHCVLDEQYF	CASSTKGPIFDHQ PQHF
CASSQGPFKAYNSPLHF	CASSYIIPICMQDTQYF	CASSQGPLNTGELFF	CASSTHAWHRQSRANVLTF
CASSQGIALRKTYGYTF	CASSYGRPHGKTYGYTF	CASSQGPFKAYNSPLHF	CASSSVIPHGKTYGYTF
CASSQGGGTYEQYF	CASSVIMRKTYGYTF	CASSQGIALRKTYGYTF	CASSSFPIFWHHQPQHF
CASSQESASGNLNTGELFF	CASSVGVGFKRGS DNEK LFF	CASSQGGGTYEQYF	CASSSRVTGRQSRANVLTF
CASSQDRLLAQHSPLHF	CASSVGNPIFMQDTQYF	CASSQESASGNLNTGELFF	CASSSPAKCHKSGQRPDF
CASSQAGVFIHEQFF	CASSVFFPICMQDTQYF	CASSQDRLLAQHSPLHF	CASSSNITRKTYGYTF
CASSPYCYRIQSRANVLTF	CASSVDTGRKTQYF	CASSQDNTGGASYEQYF	CASSMLQNRKTYGYTF
CASSPLAPIQRKNIQYF	CASSTWVISQSRANVLTF	CASSQAGVFIHEQFF	CASSSFLHWHHQ PQHF
CASSPFLHHS DNEQFF	CASSTVCPIVMQDTQYF	CASSPYCYRIQSRANVLTF	CASSRRGKTYGYTF
CASSNTGGWGYTF	CASSTPLPFVMQDTQYF	CASSPLAPIQRKNIQYF	CASSRQSPIVMQDTQYF

CASSNTGGGGYTF	CASSTKGPIFDHQPHF	CASSPFLHHSNEQFF	CASSRLVRSRKIYGYTF
CASSNTGGADYGYTF	CASSTHAWHRQSRANVLT	CASSNTGGWGYTF	CASSRHISRKTYGYTF
CASSNIPPIVMQDTQYF	CASSVIPHGKTYGYTF	CASSNTGGGGYTF	CASSQHHQPQHF
CASSNALRTGKTYGYTF	CASSRVTGRQSRANVLT	CASSNTGGADYGYTF	CASSPFNPMRKYGYTF
CASSMQINGELFF	CASSPAKCHKSGQPDF	CASSNIPPIVMQDTQYF	CASSPCATVMQDTQYF
CASSLPVPMQDTQYF	CASSNITRKYGYTF	CASSNALRTGKTYGYTF	CASSNRVATPIRTEAFF
CASSLGSRSRKIYGYTF	CASSSMLQNRKYGYTF	CASSMQINGELFF	CASSNMSIVRKYGYTF
CASSLFRTLTKIYGYTF	CASSSFAQNRKYGYTF	CASSLPVPMQDTQYF	CASSLRFMRKAYGYTF
CASSLEDPFVMQDTQYF	CASSRVPMRKYGYTF	CASSLGSRSRKIYGYTF	CASSLIDPICMQDTQYF
CASSLDRANTIYF	CASSRRLATWHHQPHF	CASSLFRTLTKIYGYTF	CASSLERTQSRANVLT
CASSLAVSGFKNIQYF	CASSRRGKTYGYTF	CASSLEDPFVMQDTQYF	CASSLCNESRKTYGYTF
CASSKYCPMQRKNIQYF	CASSRQSPVMQDTQYF	CASSLDRANTIYF	CASSLCKRSHKSRANVLT
CASSKRSHEGKIYGYTF	CASSRLVRSRKIYGYTF	CASSLAVSGFKNIQYF	CASSKMIHFHSDNEQFF
CASSKRPGSRKYGYTF	CASSRHISRKYGYTF	CASSKYCPMQRKNIQYF	CASSKLHSDNEQFF
CASSKMRPFVMQDTQYF	CASSQHHQPQHF	CASSKRSHEGKIYGYTF	CASSGVRPIFGNHQPQHF
CASSKCVPICMQDTQYF	CASSPGFKGKTYGYTF	CASSKRPGSRKYGYTF	CASSGPLRSHKSRANVLT
CASSIWLQSRANVLT	CASSPFNPMRKYGYTF	CASSKMRPFVMQDTQYF	CASSGGPICHEDTQYF
CASSHNHRQSRANVLT	CASSPCATVMQDTQYF	CASSKCVPICMQDTQYF	CASSGFISRQSRANVLT
CASSHCDPARKTYGYTF	CASSNRVATPIRTEAFF	CASSIWLQSRANVLT	CASSGEVPIKNIQYF
CASSGVLPFVMQDTQYF	CASSNMSIVRKYGYTF	CASSHNHRQSRANVLT	CASSGCSPISIHTEAFF
CASSGSSKLQSRANVLT	CASSLRFMRKAYGYTF	CASSHCDPARKTYGYTF	CASSGCEGSRKYGYTF
CASSGSKANRKYGYTF	CASSLIDPICMQDTQYF	CASSGVLPFVMQDTQYF	CASSFKLTLRKAYGYTF
CASSGRNHFIHNSPLHF	CASSLHSPFVMQDTQYF	CASSGSSKLQSRANVLT	CASSFCSPIFWHHQPHF
CASSFWVRIGKTYGYTF	CASSLGVQNRKYGYTF	CASSGSKANRKYGYTF	CASSEYLYPQSRANVLT
CASSFVLDEQYF	CASSLERTQSRANVLT	CASSGRNHFIHNSPLHF	CASSESRRHHQPQHF
CASSFSVPMQDTQYF	CASSLCNESRKTYGYTF	CASSFWVRIGKTYGYTF	CASSEHPQSRANVLT
CASSFKGASGANVLT	CASSLCKRSHKSRANVLT	CASSFVLDEQYF	CASSEGPSIYARNTIYF
CASSFIIPFVMQDTQYF	CASSKTGFKNIQYF	CASSFTSGRLLNTGELFF	CASSDVGPISDNEQFF
CASSFIFFRVFSGNTIYF	CASSKMIHFHSDNEQFF	CASSFSVPMQDTQYF	CASSDRQANRKYGYTF
CASSEINPIIHHNSPLHF	CASSGPLRSHKSRANVLT	CASSFKGASGANVLT	CASSATDPIVMQDTQYF
CASSEFKGTVSNQPQHF	CASSGGPICHEDTQYF	CASSFIIPFVMQDTQYF	CASSAPATSNKSRANVLT
CASSDMFPWHHQPHF	CASSGFISRQSRANVLT	CASSFIFFRVFSGNTIYF	CASRVCVTTQSRANVLT
CASSCTGDIYQSRANVLT	CASSGEVPIKNIQYF	CASSEINPIIHHNSPLHF	CASRTRLATHSDNEQFF
CASSASQASRKTYGYTF	CASSGCSPISIHTEAFF	CASSEFKGTVSNQPQHF	CASRLKVATWHHQPHF
CASSALLVMQDTQYF	CASSGCEGSRKYGYTF	CASSDMFPWHHQPHF	CASRIHGVQSRANVLT
CASRVQIATIIHNSPLHF	CASSFKLTLRKAYGYTF	CASSCTGDIYQSRANVLT	CASRGVLATLAHQPHF
CASRTLWQHNSPLHF	CASSEYLYPQSRANVLT	CASSASQASRKTYGYTF	CASRGSVLHSDNEQFF
CASRTGLATHTHNSPLHF	CASSEHPQSRANVLT	CASSALLVMQDTQYF	CASRFRVATLHHQPQHF
CASRNRVLHVLDEQYF	CASSEGPSIYARNTIYF	CASRVQIATIIHNSPLHF	CASRAPRKTYGYTF
CASRLFIATRCNEKLF	CASSDVGPISDNEQFF	CASRTLWQHNSPLHF	CASPSHVSRKIYGYTF
CASRKSGAPRKTYGYTF	CASSDRQANRKYGYTF	CASRTGLATHTHNSPLHF	CASKVRKYGYTF
CASRIDLAQSRANVLT	CASSDFGSSYEYF	CASRNRVLHVLDEQYF	CASKRRGVRKYGYTF
CASRFTSRTGKTYGYTF	CASSATDPIVMQDTQYF	CASRLFIATRCNEKLF	CASIRNLPKTYGYTF
CASRAPLATQRKNIQYF	CASSAPATSNKSRANVLT	CASRKSGAPRKTYGYTF	CASGSTRAARLVGDSRKTYGYTF

CASKNGEYTSRANVLTF  
CASIKGGLNTGELFF  
CASGGLAAGQSRANVLTF  
CASFGRHSRKTYGYTF  
CASALFIPGKTYGYTF  
CARQSPMVRKTYGYTF  
CAIVMQDTQYF  
CASSFTSGRLLNTGELFF  
CSARLLEREQFF  
CSARLLDFEAF  
CAWSVLDREAEQYF

CASSAFSPFVMQDTQYF  
CASRVCVTTQSRANVLTF  
CASRTRLATHSDNEQFF  
CASRNKLATVMQDTQYF  
CASRLKVATWHHPQHF  
CASRIHGVQSRANVLTF  
CASRGLATLAHQPHF  
CASRGSVLHSDNEQFF  
CASRAPRKTYGYTF  
CASPSHVSRIYGYTF  
CASKVRKTYGYTF

CASRIDLAQSRANVLTF  
CASRFTSRTGKTYGYTF  
CASRDGLAGGFKQETQYF  
CASRAPLATQRKNIQYF  
CASKNGEYTSRANVLTF  
CASIKGGLNTGELFF  
CASGGLAAGQSRANVLTF  
CASFGRHSRKTYGYTF  
CASALFIPGKTYGYTF  
CARQSPMVRKTYGYTF  
CAIVMQDTQYF

CASAPIYPRKTYGYTF  
CASSLVPTGELFF  
CASSLGGGPTGELFF  
CASSAPTGETQYF



**Supplementary Table 15: Antibodies used for immunostaining.**

Target	Isotype	Clone	Manufacturer (Cat #)	Concentration
CD3	mIgG2b	C3e/1308	Novus (NBP2-53387)	1:100
CD3	rbIgG	polyclonal	Dako (A0452),	1:150
Ki-67	rbIgG	sp6	Abcam (ab16667)	1:1000
Granzyme	ratIgG2a	496B	ThermoFisher (14-8889-82)	1:200
Granzyme	rbIgG	polyclonal	Abcam (ab53097)	1:300
Perforin	mIgG1	5B10	ThermoFisher (MA5-12469)	1:100
CD107a	mIgG1	H4A3	BioLegend (328602)	1:100
CD107a	rbIgG	D2D11	Cell Signaling (9091)	1:200
CD40L	rbIgG	D5J9Y	Cell Signaling (54535),	1:50
CD56	mIgG1	BC56C04	Biocare Medical (CM164A)	1:100
Caspase8/p43/p18	mIgG2b	2B9H8	ThermoFisher (66093-1-IG)	1:100
FOXP3	mIgG1	206D	Biolegend (320102)	1:100
Mouse IgG2a	Goat IgG	polyclonal	Invitrogen (A21135)	1:1000
Mouse IgG2a	Goat IgG	polyclonal	Invitrogen (A21241)	1:1000
Mouse IgG2b	Goat IgG	polyclonal	Invitrogen (A21147)	1:1000
Mouse IgG1	Goat IgG	polyclonal	Invitrogen (A21121)	1:1000
Rabbit IgG	Goat IgG	polyclonal	Invitrogen (A32731)	1:1000
Rabbit IgG	Goat IgG	polyclonal	Invitrogen (A21429)	1:1000
Rabbit IgG	Goat IgG	polyclonal	Invitrogen (A32733)	1:1000
Rabbit IgG	Goat IgG	polyclonal	Invitrogen (B2770)	1:1000
Biotin	Streptavidin	n/a	ThermoFisher (S21381)	1:1000

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