SUPPLEMENTARY INFORMATION

Bioinformatic Design of Dendritic Cell-Specific Synthetic Promoters

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Dr. Adam J. Brown: Email, <u>adam.brown@sheffield.ac.uk</u> Tel: +441142227505 Table S1: Highly expressed genes in monocyte-derived dendritic cells; Table S2: Highly expressed genes in conventional dendritic cells; **Table S3:** Tissue cell type specificity settings on GeneVestigator V3; Table S4: Genes exhibiting high transcriptional activity and specificity in monocyte-derived dendritic cells and conventional dendritic cells; Table S5: Genes upregulated during activation/maturation of dendritic cells; Table S6: Categorisation of relevant dendritic cell genes; Table S7: Tissue specificity and detailed matrix description filter settings on MatInspector for APC specific TFREs; Table S8: Tissue specificity and detailed matrix description filter settings on MatInspector for non-APC specific TFREs; Table S9: Offtarget cells types of off-target tissues for informatics and *in vitro* assay; Figure S1: Analysis of candidate dendritic cell-specific transcriptional factor response elements (TFREs) and transcriptional factors in monocyte-derived and myeloid dendritic cells; Figure S2: Identification of dendritic cell-specific transcriptional factors; Figure S3: Plasmid map of pVAX1-CMV-GFP; Figure S4: GFP fluorescence intensities of all homotypic promoters and the hCMV-IE1 reference promoter (CMV) in DC 2.4, C2C12, NIH-3T3 and HUVEC cells; Table S10: TFRE composition and copy number of a first library of 42 synthetic promoters; Figure S5: GFP fluorescence intensities of all 42 first library promoters and the hCMV-IE1 reference promoter (CMV) in (A) DC 2.4, (B) C2C12 and NIH-3T3, (C) Caco-2 and (D) HUVEC cells; Figure S6: Specificity of dendritic cell-specific transcriptional activity across all 42 first library promoters visualised as the minimum fold change between the relative promoter activity in DC2.4 and the relative promoter activity across all off-target cells. 11 promoters exhibiting over 5-fold changes (marked by dotted line) are identified as dendritic cell-specific promoters; Figure S7: The dendritic cell-specific TFRE activity (DCSTA) score of all 12 TFREs arranged in descending order of magnitude; Table S11: TFRE composition, copy number of a second library of 16 dendritic cell-specific synthetic promoters; Figure S8: GFP fluorescence intensities of all 16 second library promoters and the hCMV-IE1 reference promoter (CMV) in DC 2.4, C2C12, NIH-3T3 and HUVEC cells; Figure S9: A simple linear regression of dendritic cell specific promoter activity score and the observed relative promoter activities of all 27 dendritic cell-specific promoters showing a strong positive relationship between both variables.

Supplementary Tables

Gene	Mean mRNA level	STD
SNORD13	12.82909385	0.019833554
FTL	12.81008256	0.030539457
HLA-DRA	12.71935515	0.022687207
CCL22	12.64226067	0.05310759
TYROBP	12.538833	0.031129798
FTH1P8	12.5216531	0.070062705
RAB7A	12.33515827	0.016670746
GRN	12.29561328	0.026035347
MALAT1	12.22171597	0.038826023
LYZ	12.18757319	0.033674948
PSAP	12.16688414	0.002611445
LAPTM5	12.07567422	0.032336161
SLC25A6	11.99567117	0.026516769
SRGN	11.94129852	0.050420388
TMSB10	11.93426646	0.082738587
A2M	11.89327457	0.00888872
ANXA2P2	11.87314745	0.074617681
OAZ1	11.83120541	0.021382434
TXN	11.82877427	0.019515204
ATP6V0C	11.80895541	0.055630383
MRC1	11.79075018	0.086431474
PLA2G7	11.78402235	0.061951269
SPP1	11.70435942	0.066146666
ATP6V0E1	11.65368214	0.008684307
ITGAX	11.61468957	0.038858546
FTH1P7	11.56785087	0.046545406
YBX1	11.54218633	0.004389826
PLXDC2	11.49943535	0.042659063
CSTB	11.46819527	0.058868029
HLA-B	11.46657791	0.014442646
CALR	11.45100415	0.046847303
ANPEP	11.43859743	0.053405334
RF01210	11.43452348	0.081118907
GM2A	11.42517079	0.046897114
FPR3	11.41178038	0.0536685
ALOX15	11.39910845	0.04031236
CD1A	11.38504379	0.031473336

 Table S1: A1 – Genes highly expressed in monocyte-derived dendritic cells (moDC), ArrayExpress database at EMBL-EBI (www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-6192).

GLIPR1	11.35768803	0.053854828
CAPNS1	11.35647621	0.050903268
LCP1	11.34066594	0.053985991
PPT1	11.30519777	0.047041434
HIST2H2AC	11.29740247	0.039179784
ATP6V1B2	11.2846137	0.02416734
IGSF6	11.26713139	0.014139913
TUBB	11.25563173	0.046659269
SLC7A11	11.24953265	0.088179485
CTSS	11.20418681	0.060699726
EEF2	11.19994701	0.031060926
CTSC	11.18802129	0.106105711
CSDE1	11.17487798	0.004084117
PRDX1	11.16326323	0.024411849
IQGAP1	11.15854157	0.05037886
PEA15	11.15684002	0.061749477
PARP4	11.15539767	0.051879959
CD74	11.15536821	0.037297678
ATP5F1B	11.15371615	0.027546463
MOB3A	11.13417093	0.126391782
AC092573.1	11.11716193	0.033915874
CST7	11.10573724	0.145211491
SAMHD1	11.04819144	0.05727806
HLA-DMB	11.04459135	0.048702836
HMOX1	11.04298858	0.121070979
NCF2	10.99800199	0.035083902
GPNMB	10.9781378	0.052138523
GPR183	10.97190986	0.134262421
ARL6IP5	10.96683019	0.047351652
RAB31	10.95549893	0.078305513
FABP4	10.94988614	0.108421396
CTSZ	10.94683943	0.057501033
CSF1R	10.94017429	0.049116318
DAD1	10.93555656	0.075826779
GMFG	10.93311728	0.017811189
FGL2	10.9284917	0.050015122
ASAP1	10.92624379	0.041823118
HSPA8	10.92559414	0.066567253
RHOA	10.92491618	0.062192056
PKM	10.89754187	0.003455852
RPS15	10.8941833	0.028181445
UBA52	10.89254416	0.068400081

CAP1	10.87504025	0.040000286
RPL4	10.86158421	0.056148352
НЕХВ	10.85920535	0.070526851
AC018738.1	10.85772775	0.055465758
CYP1B1	10.85136126	0.048733784
CD53	10.83999796	0.035308423
ITM2B	10.83479686	0.054787878
ACTG1	10.82385507	0.009522531
ACTN4	10.81868858	0.03222306
FCER1G	10.81461242	0.067663483
ACTR2	10.7957423	0.058883459
GPX4	10.79299059	0.103733047
ATP6AP1	10.79243902	0.063185304
CD1B	10.78872106	0.109914564
CXCL16	10.76588835	0.07233349
PFN1	10.762334	0.034771034
LITAF	10.719734	0.078048179
PLEK	10.71668552	0.124052856
SLC3A2	10.71057889	0.05017224
PTBP1	10.69695775	0.018226285
GNS	10.69245304	0.025389602
MFSD12	10.59092363	0.167872234

Gene	Mean TPM	STD
MT-RNR2	42966.774	14420.97035
АСТВ	23602.422	2268.143758
FTH1	22312.567	2849.869842
FTL	17256.463	3322.378054
CD74	13926.964	5060.07214
TMSB4X	12839.941	1174.97525
EEF1A1	11998.758	1418.413392
B2M	9970.056	1841.150728
OAZ1	8892.439	4711.765554
MT-CO2	7822.693	1851.798165
MT-CO1	7242.711	964.5692788
MT-ND1	6676.426	1313.841627
MALAT1	5891.448	1642.452342
COTL1	5858.83	1526.976099
HLA-DRA	5045.631	1997.947524
MT-ND4L	4504.026	1048.344304
RPL10	4494.921	525.6296917
PSAP	4491.943	825.5429734
TPT1	4359.985	1093.530409
IFI30	3966.538	1334.489197
CST3	3486.39	914.834628
HLA-B	3434.084	1045.551338
RPL8	3408.282	819.0088507
RPS19	3398.998	884.0476649
RPL13	3356.337	362.5989013
HLA-DPA1	3283.981	855.2909276
EEF1A1P5	3265.927	1053.001141
MT-ND2	3209.876	314.1323442
RPS27	3115.577	242.3899326
PABPC1	3076.857	385.7277945
RPL41	3054.854	113.3969374
DUSP1	2897.001	1242.553889
TMSB10	2890.841	856.8382726
MT-TS1	2874.058	950.7887692
МТ-СҮВ	2857.191	315.3013425
LYZ	2837.866	1915.668424
FCGR3A	2805.037	1380.026972
MT-ND3	2729.896	1692.883829
ACTG1	2710.907	351.17409
RPL19	2680.893	280.9368966

 Table S2:
 B1 – highly expressed genes in conventional dendritic cells (cDC).¹

RPL28	2676.312	241.9280207
UBC	2604.189	1007.280844
MT-RNR1	2536.331	1090.527872
RPL26	2525.474	223.2530034
CTSS	2463.753	571.948714
TYROBP	2418.549	489.7737061
VIM	2375.781	422.0928965
RPS18	2311.133	628.5886066
HLA-C	2304.075	683.1588141
SAT1	2302.362	332.0210485
MT-ND5	2299.851	388.1322022
RPS11	2230.471	559.3492156
RPL4	2228.519	362.3731121
MT-ND4	2189.995	598.8416652
ALDOA	2178.22	514.4990156
RPL18A	2156.834	260.3224751
PFN1	2040.761	521.8521144
NAPSB	1989.478	1460.647847
RPL3	1985.305	333.2907581
RPS16	1972.806	483.7850603
GAPDH	1967.819	276.7296197
RPS23	1963.033	688.145049
RPL13A	1957.101	292.974744
MT-CO3	1941.779	488.0359058
CFL1	1937.166	331.4724289
ITM2B	1932.745	463.7466549
FCER1G	1853.647	490.5215902
RPS6	1839.882	341.7982697
GNB2L1	1772.021	260.0601655
SERPINA1	1731.143	412.223002
RPLP1	1715.837	363.6256727
RPL15	1662.473	160.9303156
RPL31	1644.151	427.5831962
SH3BGRL3	1634.711	247.9604116
RPS12	1628.5	219.0760056
RPLP2	1619.835	236.8882772
RPS3A	1619.324	322.7096218
RPS8	1615.35	220.8630282
RPS24	1578.088	532.8809178
RPL27A	1531.635	273.5495961
HLA-DPB1	1526.252	722.2324508
RPL11	1517.189	102.5195622

РТМА	1516.975	327.782518
RPS15	1499.445	306.4764055
RPL37A	1480	225.0701887
RPL17	1467.666	216.3186594
IFITM2	1462.532	391.6872604
NACA	1419.749	116.303063
MT-ATP6	1414.479	351.4040304
S100A11	1414.434	138.4340323
RPS3	1381.354	216.7214932
H3F3B	1349.338	396.7425552
LAPTM5	1324.891	315.5564936
RPS4X	1323.043	149.0322362
RPL12	1287.614	248.7468478
RPS28	1279.531	97.33175146
RPL5	1261.458	144.9402203
CORO1A	1249.319	243.250832
RPL23A	1242.916	214.4746579
ARHGDIB	1238.502	109.5347158
EIF1	1233.582	213.5154021
RPL29	1225.004	166.2150607
LSP1	1209.741	347.3706244
JUNB	1204.877	386.4596521
RPS13	1194.023	204.0626675
NFKBIA	1178.972	919.2822053
NAP1L1	1165.918	396.034932
C10orf54	1162.204	546.2711433
S100A4	1148.42	323.8930379
RPL7A	1138.249	186.4163829
FOS	1135.474	288.8276293
CD52	1124.742	302.481606
RPS17	1124.579	59.80189163
RPS29	1112.521	305.4494239
ARPC2	1106.482	194.3824432
H3F3AP4	1092.558	142.6616449
MYL6	1056.885	179.2535253
TXNIP	1052.215	305.9298604
ITGB2	1050.728	281.5828448
HLA-A	1046.889	214.517029
S100A10	1034.736	164.5005644
RPL30	1032.97	191.6999853
RPS20	1023.131	76.3241403
RPL32	1009.913	113.6199672

RPL6	1002.258	142.8519671
EEF1G	1001.328	84.77240158
IFITM3	995.563	591.6842787
MT-ND6	985.477	263.7080231
YWHAZ	970.697	298.7662475
RPS14	969.982	271.2514027
UBA52	968.321	185.2041913
RPL23	961.831	162.5918191
RPS27A	946.594	241.4911798
RPL10A	943.564	97.4258306
RPS5	911.814	137.748256
HLA-E	907.995	139.6551852
RHOA	902.827	197.538106
RPS9	900.699	189.4488818
TSC22D3	894.199	355.4597041
RPL36A	875.566	69.9132334
ARPC1B	872.763	178.1156057
RPLP0	866.41	186.1399269
S100A6	862.948	87.16276144
RPL18	854.224	80.74826286
DDX5	853.912	53.99353718
RNASEK	846.536	290.9586126
RPL18AP3	846.132	110.3611378
PTPN6	845.021	106.5266758
RPL7	842.577	186.4640208
LST1	840.022	174.2094246
MT-ATP8	838.662	131.5829353
RPL41P5	821.7465	441.2177727
TPM3	812.482	102.3043759
ANXA2	812.139	77.39971894
RPL38	798.632	168.1615573
HLA-DRB1	793.915	285.2917051
ARPC3	787.143	72.02070376
RPL39	786.506	236.4056909
RPL9P9	785.681	299.0953032
RPS28P7	781.408	162.5513959
FAU	771.415	116.8237796
PGK1	762.725	60.11768791
RPL35	759.586	101.4698555
RPL34	756.805	166.5449588
FKBP1A	753.772	135.1011024
SLC25A6	746.975	94.94690562

WARS	744.133	159.8199595
MT-TY	743.2775	800.044356
RPS15A	736.849	95.51933609
EEF1B2	730.996	68.88509576
RPL14	729.013	129.0851509
RPS25	728.099	240.1494377
H3F3A	726.656	118.7908356
CALM2	717.621	161.181487
RPL36	698.486	82.06505646
FTLP3	697.05	103.6036848
RAB11A	690.772	496.2841145
ТКТ	686.14	125.9283902
CALM1	681.81	98.33185394
GRN	679.764	177.9184477
RPL37	677.851	147.5866886
RPS10	671.389	40.07567208
HNRNPA1	662.514	115.9671781
LCP1	659.12	107.7616474
AIF1	658.334	156.0027193
TUBA1B	645.963	72.00037106
GABARAP	641.414	167.0134009
UCP2	640.251	140.7431129
RAC2	638.816	91.34319039
TCIRG1	632.557	198.1804249
FCN1	632.433	184.4935677
PTMAP5	626.776	583.7713374
KLF6	625.78	143.5839453
ZFP36	615.548	261.3214994
SARAF	615.04	151.2988339
FGR	613.805	140.3512444
RPSA	597.677	162.6314997
RPL27	596.794	105.5388368
PPIA	587.543	117.0939219
UBB	581.639	29.33642071
SELPLG	578.137	140.0763572
NFKBIZ	573.314	371.1932812
CD37	558.597	104.6241773
LINC01272	552.137	65.00657348
LILRB2	544.394	105.7245779
COX4I1	542.649	132.8564255
PFDN5	534.845	120.7706051
EIF4A1	534.734	143.3953175

GSTK1	534.546	288.6918469
PLAC8	532.769	363.0268478
CSF1R	523.616	198.5509512
PRELID1	523.101	126.4001887
SYNGR2	521.989	62.54570883
PTPRC	521.344	87.9197016
ACTR3	508.286	148.692854
EEF1D	501.968	129.8200873
НСК	500.046	61.10773636
HLA-DQB1	499.456	434.007286
DAZAP2	499.259	58.83250265
RHOG	483.404	106.8651462
ATP5B	482.594	34.12003946
RPS2	479.249	118.5444676
TAGLN2	477.225	148.8387927
FXYD5	475.876	63.72703129
RPL9	469.161	128.0937107
CD68	466.833	119.4811942
EMP3	463.214	184.5850876
CAP1	461.548	39.72004541
CFD	461.191	213.8682186
HMGN2	457.769	24.18084376
RPS21	451.567	43.08443594
SRGN	448.28	167.7409811
LRRC25	447.002	96.04187736
FLNA	446.386	153.8714904
CFP	445.869	38.78773298
STXBP2	443.39	164.6625883
FTH1P7	438.356	90.18284554
TSPO	437.186	52.29109178
HNRNPK	434.761	104.0166374
RPL41P1	428.709	377.6223588
EEF2	418.112	49.11842992
TPI1	418.092	75.90407636
LGALS1	416.813	178.563663
SERF2	416.752	113.8818348
CRIP1	415.005	120.8967234
HSPA8	410.919	158.2102742
RPS7	408.006	87.23245521
BTF3	405.886	45.00052589
ENO1	401.115	71.18225104
TUBA1A	399.995	53.91499351

SLC25A3	399.738	63.82276598
PECAM1	395.844	158.2210938
TIMP1	394.45	200.3888347
MS4A7	392.724	98.09335843
CDC37	387.8	187.2846465
YWHAB	383.839	47.5748742
PSME1	383.576	65.80713652
EIF3L	376.906	116.2921104
EEF1A1P6	374.766	87.17357652
RNH1	372.957	30.84741796
TNFRSF1B	372.325	113.6697142
S100A9	370.817	249.8898452
MTND2P28	369.15	108.0809397
RNASET2	365.613	82.43609924
RPL13AP5	364.93	91.79719515
RPL3P4	360.173	345.8144113
RPL35A	359.274	117.8652023
RPL21	357.689	64.28564949
MYD88	356.41	40.75486336
ANXA5	354.614	50.88584201
MIR3064	352.805	410.4843965
LILRA1	351.764	77.53233796
CD44	349.701	53.64455289
UQCRC1	345.322	63.90300322
GMFG	343.255	209.6021637
GSTP1	340.212	76.0784713
ADGRE5	339.165	39.22627579
HCLS1	337.611	57.17858585
ASAH1	336.629	69.36020314
SRSF5	334.098	61.6364059
CNBP	332.278	35.11398628
RHOC	331.783	56.57244102
MYL12A	326.111	86.56905483
MSN	326.036	77.13287491
CLIC1	325.363	73.46900559
CTSH	321.403	102.6468551
ARF1	318.352	52.98826316
CTSB	318.019	52.78118964
NPC2	317.263	80.68432868
RGS19	312.725	78.69306299
MT-TQ	306.963	636.5700552
CCNI	300.48	108.5921367

RPL24	295.087	104.8358908
PYCARD	292.803	47.78565234
MT-TN	291.007	155.4957792
CD48	290.036	55.88341675
TMBIM6	288.69	61.35639952
CTSD	285.362	104.128723
CPVL	284.087	129.68021
SIGLEC10	282.607	101.8507773
CD53	281.285	77.61424966
LIMD2	277.98	79.70791115
SLC25A5	272.158	54.80868392
ATP5G2	272.019	73.2911407
PGAM1	270.935	22.76309486
EIF3F	268.597	46.01024894
PTP4A2	267.324	57.81571104
GDI2	265.049	64.69550317
CCND3	261.134	79.32295344
BID	260.933	31.67813769
PILRA	260.582	26.70503525
MYL12B	257.382	15.34261329
SPN	256.609	33.67900448
ZFP36L1	256.409	135.1624944
PPP1CA	254.65	13.2836756
ATP6V0B	253.126	23.01402871
HLA-DQA1	250.483	122.9385742
SLC11A1	248.485	65.07453294
MYO1F	247.207	60.34528757
M6PR	245.988	51.51361356
NME2	245.784	22.88393634
CAPZB	245.305	20.48321325
ARPC5	244.365	60.84653061
HLA-F	242.502	141.1998471
LDHA	242.316	44.77327264
HLA-DRB5	240.386	182.494776
EIF5A	240.231	42.63392478
C1orf162	237.759	36.4618188
ANXA1	237.203	93.36220124
EIF3K	236.913	52.59056683
GPX4	235.382	27.89436068
MT-TL1	232.734	152.4164751
LILRB1	232.662	67.81292932
LILRA5	231.535	84.35525658

COX7C	229.809	57.08853085
PRR13	229.577	40.61869068
CTSC	229.539	51.20306478
PTMAP2	228.379	83.78501159
LY6E	226.575	93.74953
CMTM6	226.129	35.72681038
ATP5A1	226.128	67.28538601
AP1S2	225.289	61.95950607
CNN2	224.757	43.19310747
ATP5L	224.755	58.27021774
ZFAND5	223.177	64.22947256
RBM3	220.725	42.33726063
LGALS9	217.434	76.71170131
RNF130	214.986	22.58902593
RPS3AP6	214.627	88.40512362
МТ-ТК	214.285	293.4270925
PTGES3	213.152	18.03307572
THEMIS2	213.035	51.41989875
GNG5	212.86	47.00170529
ARPC4	211.813	40.17305029
CANX	210.54	110.5558746
IER2	210.321	69.33293656
NPM1	210.021	61.52320887
SLC44A2	208.954	77.65790844
PPT1	207.154	48.64952433
ID2	206.266	32.60451146
MT-TE	205.557	200.0159337
HNRNPDL	205.209	38.58289945
FCGRT	204.861	35.16592801
EIF3H	204.307	38.3162982
ZYX	202.838	61.723497
COX5A	202.532	25.83490459
RAP1B	202.223	44.72667543
IL16	202.039	89.29424263
AMPD2	199.901	76.58821012
СКВ	198.72	87.37614592
LAMTOR4	197.929	43.94854796
LGALS3	195.918	26.91009165
ATG3	195.773	43.29726227
PPP1R15A	194.7075	82.73655586
NINJ1	194.687	68.89701042
MTATP6P1	194.296	66.26750999

ATP1B3	193.132	11.41380338
TALDO1	192.716	28.85840311
FCGR3B	191.628	282.081323
ITGA4	191.303	53.97940922
LYPD2	190.083	73.48505814
PSMB8	189.751	39.44031478
РКМ	189.082	40.01716516
HMOX1	188.489	38.23212318
НКЗ	187.794	19.59063022
FAM26F	186.825	101.5140354
CD4	186.756	25.51471791
PPIAP22	186.394	65.33823167
FLII	186.336	36.60852981
ITGAX	185.884	37.2570192
LRRFIP1	185.389	45.52638293
GLIPR1	183.732	28.31202077
SHKBP1	183.566	33.15337566
TPP1	183.307	42.34351081
BIN2	182.147	32.46568893
GPX1	181.902	63.5262592
SLC7A7	181.867	36.96713838
PGLS	181.61	38.89497365
HNRNPA2B1	178.462	29.0941458
HLA-DMA	178.214	88.53689664

For some of the specificity settings on Och vestigation via					
Expressed in	Not expressed in				
Monocyte derived dendritic cells	Blood outgrowth endothelium				
	Blood vessel vascular endothelium				
	Microvascular endothelium				
	Lymphatic microvessel endothelium				
	Skin fibroblast				
	Dermal microvessel endothelium				
	Epidermal keratinocyte				
	Dermal fibroblast				
	Monocyte derived microphage				
	Skeletal muscle myoblast				
	Skeletal muscle myotube				
	Myoblast derived myotube				
	Synovial fibroblast				
Conventional dendritic cells	Blood vessel vascular endothelium				
	Dermal microvessel endothelium				
	Epidermal keratinocyte				
	Dermal fibroblast				
	Monocyte derived microphage				
	Skeletal muscle myoblast				
	Skeletal muscle myotube				
	Myoblast derived myotube				
	Joint synovial fibroblast				

Table S3: Tissue cell type specificity settings on GeneVestigator V3²

Cell type	Gene
Monocyte-derived dendritic cells	CCL22
	ALOX15
	NCF2
	CD1A
	CD74
	TYROBP
	HLA-DRA
	L CD1
	EDD 2
	ГГК <u>Ј</u>
	CSE1R
Conventional dendritic cells	CPVI
	ITGB2
	AMPD2
	COTL1
	VSIR
	CD48
	FGR
	STXBP2
	MYO1F
	THEMIS2
	HCLS1
	CD74
	SPN
	TNFRSF1B
	FOS
	SELPLG
	DI AC9
	L RRC25
	RNASET2
	Clorf162
	CFP
	НІ А ДРА
	ECN1
	FCNI
	RGS19
	PTPN6
	ADGRE5
	HLA-DPA1
	ITGAX
	HLA-DMA
	HLA-DPB1

Table S4: Genes exhibiting high transcriptional activity and specificity in monocyte-derived dendritic cells and conventional dendritic cells ²

Gene	Ensembl ID	Gene ID
AZI2	ENSG00000163512	64343
B3GNT2	ENSG00000170340	10678
CCDC50	ENSG00000152492	152137
CCL2	ENSG00000108691	6347
CCL4	ENSG00000129277	6351
CD200	ENSG0000091972	4345
CD38	ENSG0000004468	952
CD80	ENSG00000121594	941
CD86	ENSG00000114013	942
CFB	ENSG00000243649	629
CFLAR	ENSG0000003402	8837
CLIC4	ENSG00000169504	25932
CXCL10	ENSG00000169245	3627
CXCL9	ENSG00000138755	4283
DNAJA2	ENSG0000069345	10294
DUSP2	ENSG00000158050	1844
EIF2AK2	ENSG0000055332	5610
FSCN1	ENSG0000075618	6624
GADD45B	ENSG0000099860	4616
GBP2	ENSG00000162645	2634
GCH1	ENSG00000131979	2643
GPD2	ENSG00000115159	2820
IFI44	ENSG00000137965	10561
IFIH1	ENSG00000115267	64135
IFIT2	ENSG00000119922	3433
IFIT3	ENSG00000119917	3437
IL15	ENSG00000164136	3600
IL15RA	ENSG00000134470	3601
IL2RA	ENSG00000134460	3559
IL6	ENSG00000136244	3569
IRF1	ENSG00000125347	3659
ISG20	ENSG00000172183	3669
JDP2	ENSG00000140044	122953
LTA	ENSG00000226979	4049
MARCKSL1	ENSG00000175130	65108
MX1	ENSG00000157601	4599
NCK2	ENSG0000071051	8440
NFKBIA	ENSG00000100906	4792
NMI	ENSG00000123609	9111
NT5C3	ENSG00000122643	51251

Table S5: 72 C - Genes upregulated during activation/maturation of dendritic cells.³

OAS2	ENSG00000111335	4939
OASL	ENSG00000135114	8638
PARP9	ENSG00000138496	83666
PELI1	ENSG00000197329	57162
PI4K2B	ENSG0000038210	55300
PLA1A	ENSG00000144837	51365
PML	ENSG00000140464	5371
PTGS2	ENSG0000073756	5743
RBBP8	ENSG00000101773	5932
REL	ENSG00000162924	5966
RGS1	ENSG0000090104	5996
RIPK2	ENSG00000104312	8767
RSAD2	ENSG00000134321	91543
RTP4	ENSG00000136514	64108
SDC4	ENSG00000124145	6385
SERPINB9	ENSG00000170542	5272
SOS1	ENSG00000115904	6654
STAT1	ENSG00000115415	6772
STAT2	ENSG00000170581	6773
TANK	ENSG00000136560	10010
TAP1	ENSG00000168394	6890
TDRD7	ENSG00000196116	23424
TLK2	ENSG00000146872	11011
TMCC3	ENSG0000057704	57458
TNFAIP3	ENSG00000118503	7128
TNFSF10	ENSG00000121858	8743
TNFSF4	ENSG00000117586	7292
TNFSF9	ENSG00000125657	8744
TRAF1	ENSG0000056558	7185
TRIM21	ENSG00000132109	6737
UBE2L6	ENSG00000156587	9246
XRN1	ENSG00000114127	54464
ZNF281	ENSG00000162702	23528

Table 50:	Categorisation of relevant dendritic cell genes	
Gene Class Nomenclature	Gene Type	Number of genes
A1	Highly expressed in moDC	100
A2	Highly specific to moDC	100
A1-2	Highly expressed moDC-specific gene	12
B1	Highly expressed in cDC	400
B2	Highly specific to cDC	400
B1-2	Highly expressed cDC-specific gene	33
С	Upregulated in moDC & cDC	64

Table S6: Categorisation of relevant dendritic cell genes

Table S7: Tissue specificity and detailed matrix description filter settings on MatInspector for APC specific TFREs

Contains	AND	Does not contain (ANY)
Antigen presenting cells		Skeletal muscles
		Skeletal
		Connective tissue
		Repressor
		Repressing
		Suppressor

Table S8: Tissue specificity and detailed matrix description filter settings on MatInspector for non-APC specific TFREs

	specific 111115								
Contains (ANY)	OR	Does not contain (ANY)							
Skeletal muscles		Antigen presenting cells							
Skeletal		Leukocytes							
Connective tissue		PU.1							
Repressor									
Repressing									
Suppressor									
Ubiquitous									

Table S9: Off-target cells types of off-target tissues for informatics and *in vitro* assay

Tissue	Cell types	Cell line for assay
Skeletal muscle tissue	Skeletal muscle	C2C12
	Skeletal muscle superior quadracep	
Connective tissue	Differentiated myofibroblast	NIH-3T3
	Skin cultured fibroblast	
	Skin fibroblast	
Endothelium	Microvascular endothelial cell	HUVEC
	Lymphatic vessel endothelial cell	
Epithelium	Skin epithelial cell keratinocyte	CaCO-2

Figure S1. Analysis of candidate dendritic cell-specific transcriptional factor response elements (TFREs) and transcriptional factors in monocyte-derived and myeloid dendritic cells (A) Identification of 745 transcriptional factor regulatory sequences (TFREs) over-represented in the promoter regions of target genes (highly expressed genes specific to the target cell types: monocyte derived dendritic cells (moDC), conventional/myeloid dendritic cells (cDC) and genes which are upregulated during dendritic cell activation/maturation), using the common TF tool of Genomatix, *p* value < 0.005. (B) Identification of 52 TFRES of transcriptional factors (TFs) unique to antigen presenting cells (APCs) in the promoter region of target genes, using the MatInspector tool of Genomatix. (C) Identification of 170 transcriptional factors highly expressed in the target cell types (moDC, cDC, and mature/activated myeloid/conventional dendritic cells (mmDC). (D) Selection of 79 candidate TFs which are relatively highly expressed in the target cell types compared to the off-target cell types (myocytes, fibroblast, endothelial and epithelial cells).



170 TFs across Mo-DC, myeloid DC, activated myeloid DC

79 signature DC TF candidates

Figure S2. Identification of dendritic cell-specific transcriptional factors (A) Identification of 69 core transcriptional factors (TFs) with high regulatory potential in target cell types: monocyte-derived, conventional and activated dendritic cells (TSSQ cut-off > 0.1) using the Target Score Specificity Quotient (TSSQ) parameter *i.e.* the normalised difference of mean specificity score (1-1-100) of each of the 79 core TFs in the off-target and target cell types *i.e.* difference between the mean specificity score of each TF in all off-target cell types (MBSS) and the mean specificity score of each TF in all target cell types (MTSS) normalised the highest difference value. (B) Selection of 10 TFs with TSSQ > 0.1 and high regulatory potential in target cell types (using TFdiff encode (p value <0.05), Ingenuity Pathway Analysis, and the Human Protein Atlas) from a selection of transcriptional factor regulatory sequences (TFREs) which are common to a population of 745 over-represented TFREs in the promoters of target genes, 52 TFREs of TFs peculiar to antigen presenting cells (APCs), and all TFREs of the 69 core transcriptional factors found in the promoter region of target genes. (C) Classification of the 10 selected TFs based of TSSQ value (D) The mean of the mean specificity score of all 10 selected TFs in the off-target/base cell types and target cell types indicates that the selected TFs are unique to the target cell types (two-tailed independent t test, p value < 0.0001).



Figure S3: Plasmid map of pVAX1-CMV-GFP



Figure S4: GFP fluorescence intensities of all homotypic promoters and the hCMV-IE1 reference promoter (CMV) in DC 2.4, C2C12, NIH-3T3 and HUVEC cells. Values represent the mean \pm standard deviation across three independent transfections each performed in triplicate.



PROMOTER	IRF8-A	IRF9-A	RELA-A	BATF-A	JUNB-A	c-Rel-A	SPI1-A	STAT5A-A	c-Rel-B	BATF-B	IRF4-B	IRF4-A
1/01	0	0	0	2	0	0	10	0	0	0	0	4
1/02	0	0	2	0	0	2	2	0	2	2	14	2
1/03	0	0	0	0	0	4	4	0	0	2	10	0
1/04	0	6	2	0	0	6	6	0	0	6	12	0
1/05	0	0	0	0	6	0	0	6	0	0	0	6
1/06	0	0	0	0	0	6	6	0	0	0	6	0
1/07	0	0	0	0	0	6	6	0	0	2	6	0
1/08	0	0	0	2	0	6	6	0	0	0	0	6
1/09	2	0	0	0	4	0	10	0	0	0	0	4
1/10	0	0	6	0	4	0	6	4	0	0	0	0
1/11	0	0	0	0	0	0	2	0	2	2	6	2
1/12	0	0	0	0	0	6	0	0	0	6	6	2
1/13	0	4	0	0	6	0	4	0	0	0	0	6
1/14	0	6	0	0	0	0	6	0	0	2	6	0
1/15	0	0	0	0	0	2	2	0	0	0	2	2
1/16	0	6	2	0	0	8	2	0	2	2	8	0
1/17	4	0	0	10	4	0	0	0	0	0	0	4
1/18	2	0	0	0	4	10	0	0	0	0	0	4
1/19	0	4	0	0	0	2	4	0	0	2	6	2
1/20	0	6	2	0	0	0	6	0	0	0	6	0
1/21	2	0	0	0	4	10	0	4	0	0	0	0
1/22	0	0	0	0	6	4	4	6	0	0	0	0
1/23	0	4	2	0	0	0	4	0	0	0	6	2
1/24	2	0	0	0	6	6	6	0	0	0	0	0
1/25	0	2	0	0	0	6	0	0	0	6	6	0

Table S10. TFRE composition and copy number of a first library of dendritic cell-specific synthetic promoter candidates

1/26	6	0	0	4	4	0	6	0	0	0	0	0
1/27	0	10	0	2	0	0	0	4	0	0	0	4
1/28	0	6	0	0	0	6	6	0	0	0	0	0
1/29	0	10	0	2	4	0	0	0	0	0	0	4
1/30	6	4	0	0	6	0	6	0	0	0	0	0
1/31	6	0	0	0	4	4	6	0	0	0	0	0
1/32	0	6	0	2	0	0	6	0	0	0	0	6
1/33	2	6	0	0	6	6	0	0	0	0	0	0
1/34	0	10	2	0	4	0	0	4	0	0	0	0
1/35	10	0	0	2	4	0	0	4	0	0	0	0
1/36	0	6	2	0	0	0	6	0	0	0	0	6
1/37	2	6	0	0	0	6	0	6	0	0	0	0
1/38	6	0	6	6	0	0	0	0	0	0	0	0
1/39	0	6	2	0	0	0	4	0	2	2	2	4
1/40	0	4	2	0	0	0	2	0	0	0	4	0
1/41	0	12	2	0	0	2	4	0	0	0	2	8
1/42	8	0	0	2	2	0	2	0	0	0	0	2

Figure S5: GFP fluorescence intensities of all 42 first library promoters and the hCMV-IE1 reference promoter (CMV) in (A) DC 2.4, (B) C2C12 and NIH-3T3, (C) Caco-2 and (D) HUVEC cells. Values represent the mean \pm standard deviation across three independent transfections each performed in triplicate.



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Figure S6: Specificity of dendritic cell-specific transcriptional activity across all 42 first library promoters visualised as the minimum fold change between the relative promoter activity in DC2.4 and the relative promoter activity across all off-target cells. 11 promoters (starred) exhibiting over 5-fold changes (marked by dotted line) are identified as dendritic cell-specific promoters.



Figure S7: The dendritic cell-specific TFRE activity (DCSTA) score of all 12 TFREs arranged in descending order of magnitude.



Promoter	IRF9-A	RELA-A	c-Rel-A	SPI1-A	c-Rel-B	BATF-B	IRF4-B	IRF4-A	BATF-A
2/01	0	0	4	1	2	0	2	4	2
2/02	1	0	0	2	0	0	2	0	0
2/03	2	2	0	0	0	0	2	0	0
2/04	2	0	0	0	2	0	2	0	0
2/05	2	0	0	0	0	2	2	0	0
2/06	4	2	2	0	2	0	2	0	0
2/07	4	2	0	1	2	0	2	4	0
2/08	4	2	2	0	2	0	4	0	0
2/09	4	2	4	0	2	0	2	0	0
2/10	4	2	0	3	2	0	2	6	0
2/11	4	0	0	2	2	0	4	0	0
2/12	5	2	0	4	0	2	2	4	0
2/13	4	2	4	2	2	0	2	2	0
2/14	5	2	2	4	2	0	0	4	0
2/15	5	2	0	4	2	2	0	4	0
2/16	4	2	0	2	0	2	2	4	0

Table S11. TFRE composition, copy number of a second library of 16 dendritic cell-specific promoters.

Figure S8: GFP fluorescence intensities of all 16 second library promoters and the hCMV-IE1 reference promoter (CMV) in DC 2.4, C2C12, NIH-3T3 and HUVEC cells. Values represent the mean \pm standard deviation across three independent transfections each performed in triplicate.



Figure S9. A simple linear regression of dendritic cell specific promoter activity score and the observed relative promoter activities of all 27 dendritic cell-specific promoters showing a strong positive relationship between both variables.



DC-SPECIFIC PROMOTER SEQUENCES

Colour code

TFRE	Colour
IRF9-A	Orange
IRF4-B	Blue
IRF4-A	Gold
SPI1-A	Purple
BATF-B	Blue-Grey
c-Rel-A	Grey
c-Rel-B	Light-Green
RELA-A	Red
BATF-A	Light-Blue
SPACERS	Black

1.1/36 - 471 bp

2.1/39 - 454 bp

3.1/15 - 177 bp

CTTGGGGTTTCCAACCTTGGGGTTTCCAACGTAGATGTGGAAGTGAAAGCTACAAGTAGATG TGGAAGTGAAAGCTACAAATAGGAGGGCTAAAGAAAGCAGAAAACTATAGGAGGGCTAAAGA AAGCAGAAAGTGAAGGAGGAAGTCTGAGGCTTGTGAAGGAGGAAGTCTGAGGC

4.1/40 - 274 bp

CTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAACTAAGCTGTAGATGTGGAA GTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAACTAAACCGAGAATCGAAACTAAGC TCTAAACCGAGAATCGAAACTAAGCTGAAGGACTTTCCAGCGAAGGACTTTCCAGCGTAGAT GTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAAGTGAAGGAGGAAGTCTGA GGCTTGTGAAGGAGGAAGTCTGAGGC

5.1/06 - 374 bp

CTTGGGGTTTCCAACCTTGGGGTTTCCAACGTAGATGTGGAAGTGAAAGCTACAAGTAGATG TGGAAGTGAAAGCTACAAGTGAAGGAGGAGGAAGTCTGAGGCTTGTGAAGGAGGAAGTCTGAGGC GTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAAGTGAAGGAGGAA GTCTGAGGCTTGTGAAGGAGGAAGTCTGAGGCCTTGGGGGTTTCCAACCTTGGGGTTTCCAAC GTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAACTTGGGGTTTCC AACCTTGGGGGTTTCCAACAAGTGAAGGAGGAAGTCTGAGGC**TT**GTGAAGGAGGAAGTCTGAG GC

6.1/16 - 600 bp

7.1/07 - 400 bp

CTTGGGGTTTCCAACCTTGGGGTTTCCAACGTAGATGTGGAAGTGAAAGCTACAAGTAGATG TGGAAGTGAAAGCTACAACTTGGGGGTTTCCAACCTTGGGGTTTCCAACTCTTGACTCAGTCT CTTGACTCAGTCGTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAA GTGAAGGAGGAAGTCTGAGGCTTGTGAAGGAGGAAGTCTGAGGCCTTGGGGGTTTCCCAACCTT GGGGTTTCCAACTTGTGAAGGAGGAAGTCTGAGGCTTGTGAAGGAGGAAGTCTGAGGCGTAG ATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAGGCTACAAGTGAAGGAGGAAGTCT GAGGCTTGTGAAGGAGGAAGTCTGAGGC

8.1/11 - 303 bp

GTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAACAGGGTGGTTCC TTCCAGGGTGGTTCCTTCGTAGATGTGGAAGTGAAAGCTACAAGTAGAAG CTACAATCTTGACTCAGTCTCTTGACTCAGTCGTAGATGTGGAAGTGAAAGCTACAAGTAGA TGTGGAAGTGAAAGCTACAAATAGGAGGGCTAAAGAAAGCAGAAAACTATAGGAGGGCTAAA GAAAGCAGAAAGTGAAGGAGGAAGTCTGAGGCCTTGTGAAGGAGGAAGTCTGAGGC

9.1/12 - 318 bp

CTTGGGGGTTTCCAACCTTGGGGTTTCCAACGTAGATGTGGAAGTGAAAGCTACAAGTAGATG TGGAAGTGAAAGCTACAATCTTGACTCAGTCTCTTGACTCAGTCCTTGGGGTTTCCAACCTT GGGGTTTCCAACTCTTGACTCAGTCTCTTGACTCAGTCGTAGATGTGGAAGTGAAAGCTACA AGTAGATGTGGAAGTGAAAGCTACAATCTTGACTCAGTCTCTTGACTCAGTCCTTGGGGTTT CCAACCTTGGGGTTTCCAACGTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAA AGCTACAA

10. 1/23 - 451 bp

CTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAACTAAGCTGTAGATGTGGAA GTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAACTAAACCGAGAATCGAAACTAAGC TCTAAACCGAGAATCGAAACTAAGCTGAAGGACTTTCCAGCGAAGGACTTTCCAGCGTAGAT GTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGGAAAGCTACAACTTGGGGGTTTCCAACCTT GGGGTTTCCAACGTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAA GTGAAGGAGGAAGTCTGAGGCTTGTGAAGGAGGAAGTCTGAGGCATAGGAGGGCTAAAGAAA GCAGAAAACTATAGGAGGGCTTAAAGAAAGCAGAAAGTGAAGGAGGAAGTCTGAGGCTTGTGA AGGAGGAAGTCTGAGGC

11. 1/19 - 449 bp

12. 2/13 - 367 bp

13. 2/01 - 295 bp

14. 2/04 - 130 bp

CTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAACTAAGCTCAGGGTGGTTCC TTCCAGGGTGGTTCCTTCGTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAG CTACAA

15. 2/07 - 337 bp

16. 2/10 - 434 bp

17. 2/16 - 356 bp

CTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAACTAAGCTATAGGAGGGGCTA AAGAAAGCAGAAAACTATAGGAGGGGCTAAAGAAAGCAGAAACTAAACCGAGAATCGAAACTA AGCTCTAAACCGAGAATCGAAACTAAGCTGAAGGACTTTCCAGCGAAGGACTTTCCAGCTCT TGACTCAGTCTCTTGACTCAGTCGTAGATGTGGAAGGAGTGAAAGCTACAAGTAGATGTGGAAGT

18. 2/12 - 425 bp

ctaaaccgagaatcgaaactaagctctaaaccgagaatcgaaactaagctataggaggggcta aaGAAAgcagaaaACTataggagggctaaaGAAAgcagaaactaaaccgagaatcgaaacta agctctaaaccgagaatcgaaactaagctgaaggactttccAGCGAAGGACTTTCCAGCtct tgactcagtctcttgactcagtcgtagatgtggaagtgaaagctacaagtagatgtggaagt gaaagctacaaCTAAACCGAGAATCGAAACTAAGctgtgaaggaggaagtctgaggcTTgtg aaggaggaagtctgaggcataggagggctaaaGAAAgcagaaaACTataggagggctaaaGA AAgcagaaagtgaaggaggaagtctgaggcTTgtgaaggaggaagtctgaggc

19. 2/09 - 270 bp

20. 2/06 - 240 bp

CTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAACTAAGCTCAGGGTGGTTCC TTCCAGGGTGGTTCCTTCCTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAAC TAAGCTCTTGGGGTTTCCAACCTTGGGGTTTCCAACGAAGGACTTTCCAGCGAAGGACTTTC CAGCGTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAA

21. 2/05 - 126 bp

CTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAACTAAGCTTCTTGACTCAGT CTCTTGACTCAGTCGTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTAC AA

22. 2/02 - 119 bp

CTAAACCGAGAATCGAAACTAAGCTGTGAAGGAGGAGGAAGTCTGAGGCTTGTGAAGGAGGAAGT CTGAGGCGTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAGCTACAA

23. 2/03 - 130 bp

CTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAACTAAGCTGAAGGACTTTCC AGCGAAGGACTTTCCAGCGTAGATGTGGAAGTGAAAGCTACAAGTAGATGTGGAAGTGAAAG CTACAA

24. 2/11 - 280 bp

CTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGAATCGAAACTAAGCTGTGAAGGAGGAA GTCTGAGGCTTGTGAAGGAGGAAGTCTGAGGCGTAGATGTGGAAGTGAAAGCTACAAGTAGA TGTGGAAGTGAAAGCTACAAACGCGTCTAAACCGAGAATCGAAACTAAGCTCTAAACCGAGA ATCGAAACTAAGCTCAGGGTGGTTCCTTCCAGGGTGGTTCCTTCGTAGATGTGGAAGTGAAA GCTACAAGTAGATGTGGAAGTGAAAGCTACAA

25. 2/08 - 296 bp

26. 2/15 - 405 bp

27. 2/14 - 409 bp

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