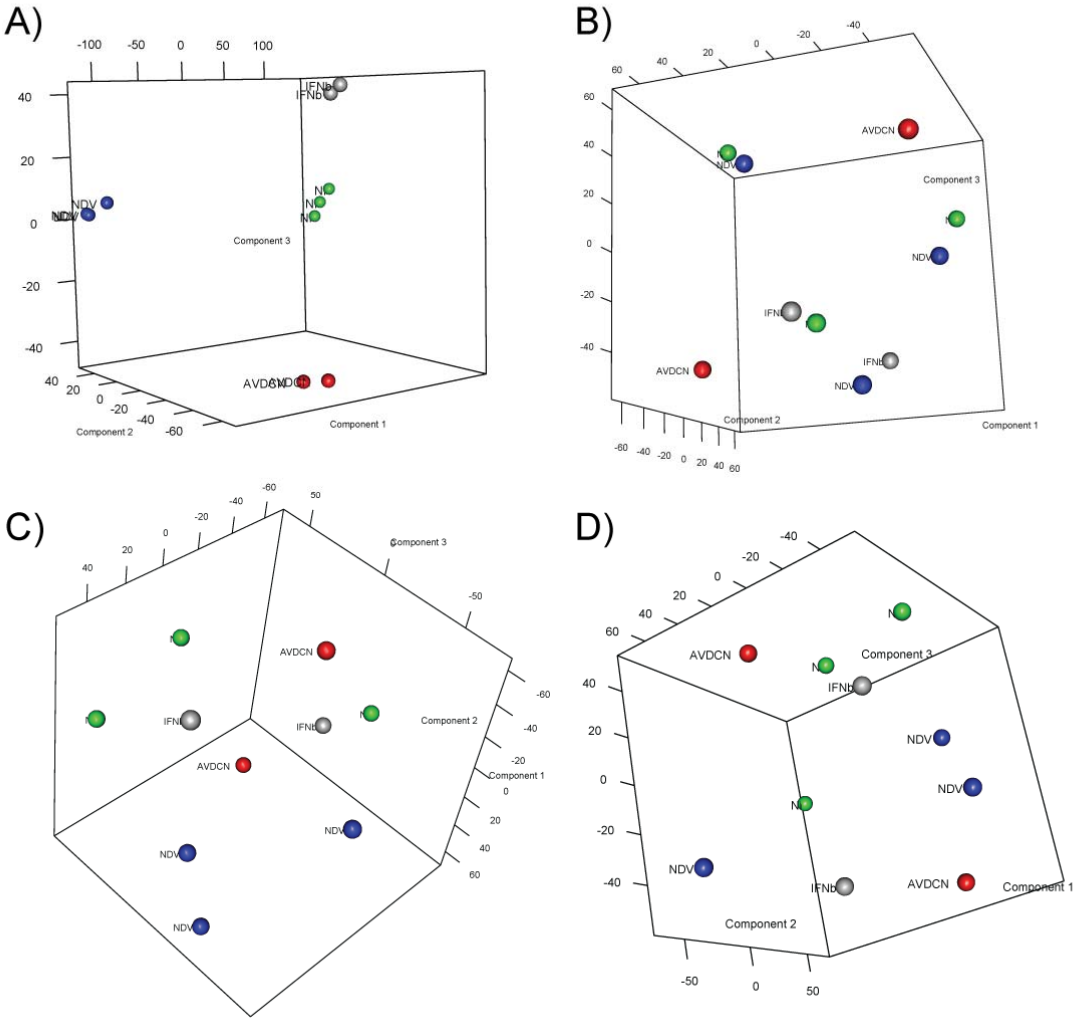


**Figure S1: Robustness analysis of PCA.** Randomized design is generally considered as one the most robust evaluation methodologies. We used it here to evaluate the robustness of the PCA analysis. An expression vector for each probe ID was randomly shuffled and the PCA analysis was repeated on the randomize data. The scores of the first three components of the PCA based on the original are depicted in Fig S1A and and on the randomized data S1B, S1C and S1B correspondingly.

To test for robustness we used the statistical MANOVA analysis to test for presence of clusters both in our and in the randomized data set. Our null hypothesis was that the data doesn't contain any clusters. Formally, we tested to see if the vector of values of the dependent variables (coordinates) is equal for multiple independent groups (samples) and our null hypothesis would be:

$$H0 : \begin{pmatrix} X11 \\ Xp1 \end{pmatrix} = \begin{pmatrix} X12 \\ Xp2 \end{pmatrix} = \ldots = \begin{pmatrix} X1k \\ Xpk \end{pmatrix},$$

where p represents the total number of dependent variables (coordinates) for k levels (samples). The Wilks test for indicated that the null hypothesis can be rejected with p-value of 5.08e-15, indicating the presence of clusters in the data. The same test on the randomized data fails to rejects the null hypothesis (p-value of 0.472), indicating that the randomized data set doesn't include clusters.

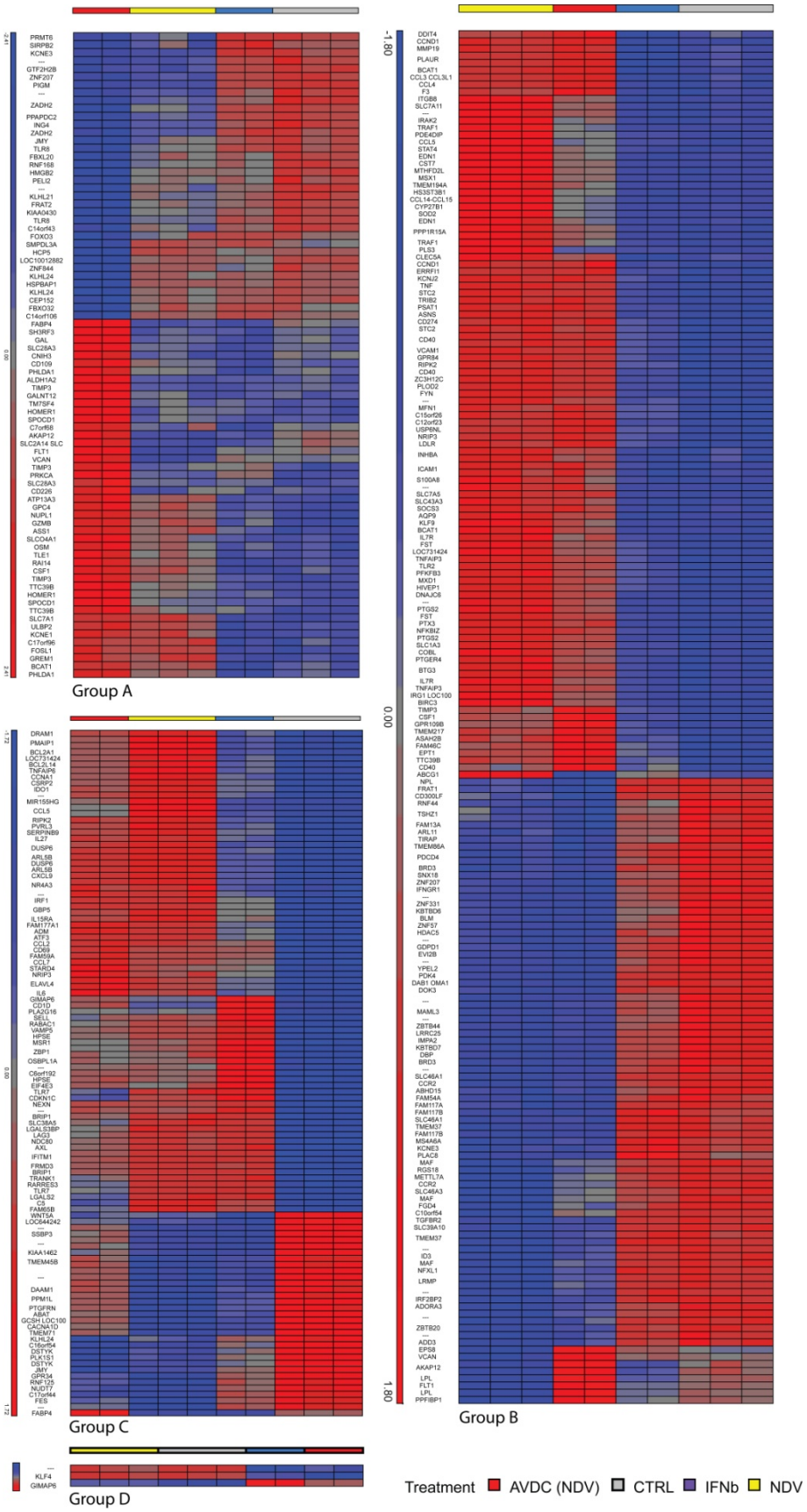


**Figure S2: Transcripts which showed a significant change between exposure to paracrine signaling and single cytokine IFNb treatment**. Group (A): Transcripts significantly altered by the paracrine signaling that did not show significant induction by NDV infection or IFNb treatment when compared to control. Group (B): Transcripts significantly induced by paracrine signaling and NDV infection but not IFNb treatment when compared to control. Group (C): Transcripts significantly induced by paracrine signaling, NDV infection and IFNb treatment when compared to control. Group (D): Transcripts significantly altered by paracrine signaling and IFNb treatment when compared to control that also differed significantly between exposure to paracrine signaling and IFNb treatment.

**Table S1: Pair wise comparisons for CD86 of DCs treated in all combinations with IFNβ, TNFα and IL1b**. Pair wise comparisons were calculated with ANOVA followed by Tukey's 'Honest Significant Difference' method.

| | CD86 1:1 | | | | CD86 1:2 | | | | CD86 1:4 | | | | CD86 1:8 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | diff | lwr | upr | p adj | diff | lwr | upr | p adj | diff | lwr | upr | p adj | diff | lwr | upr | p adj |
| IFNb/IL1b-IFNb | 1523 | 837.02 | 2208 | 9.57E-06 | 1222 | -84.49 | 2528 | 0.076964 | 1181 | 945.4 | 1417 | 1.51E-11 | 732.88 | 233.68 | 1232.1 | 0.001743 |
| IL1b-IFNb | -644 | -1329 | 41.82 | 0.075132 | -771 | -2078 | 534.7 | 0.505333 | -833 | -1069 | -597 | 6.65E-09 | -842.91 | -1342.1 | -343.71 | 0.000356 |
| null-IFNb | -1418 | -2012 | -825 | 3.32E-06 | -1296 | -2427 | -165 | 0.018106 | -1229 | -1433 | -1025 | 4.85E-13 | -1122.6 | -1554.9 | -690.29 | 9.46E-07 |
| TNFa-IFNb | -215 | -900.6 | 470.5 | 0.957043 | -463 | -1769 | 843.6 | 0.921991 | -975 | -1210 | -739 | 4.60E-10 | -761.11 | -1260.3 | -261.92 | 0.001155 |
| TNFa/IFNb-IFNb | 2946 | 2260.6 | 3632 | 2.34E-10 | 2128 | 821.83 | 3434 | 0.000544 | 454.4 | 218.5 | 690.2 | 6.76E-05 | 221.26 | -277.94 | 720.45 | 0.797043 |
| TNFa/IL1b-IFNb | 1721 | 1035.1 | 2406 | 1.59E-06 | 1303 | -2.767 | 2610 | 0.050723 | -82.5 | -318 | 153.4 | 0.926641 | -386.8 | -885.99 | 112.4 | 0.206002 |
| TNFa/IL1b/IFNb-IFNb | 2642 | 1956.1 | 3327 | 1.51E-09 | 2741 | 1435.2 | 4048 | 2.12E-05 | 2665 | 2429 | 2901 | 0 | 1867 | 1367.8 | 2366.2 | 2.52E-09 |
| IL1b-IFNb/IL1b | -2166 | -2852 | -1481 | 4.21E-08 | -1993 | -3299 | -687 | 0.001145 | -2014 | -2250 | -1778 | 0 | -1575.8 | -2075 | -1076.6 | 4.29E-08 |
| null-IFNb/IL1b | -2941 | -3534 | -2347 | 1.86E-11 | -2518 | -3649 | -1386 | 9.29E-06 | -2410 | -2614 | -2206 | 0 | -1855.5 | -2287.8 | -1423.2 | 2.39E-10 |
| TNFa-IFNb/IL1b | -1738 | -2423 | -1052 | 1.37E-06 | -1684 | -2990 | -378 | 0.006411 | -2156 | -2392 | -1920 | 0 | -1494 | -1993.2 | -994.79 | 1.02E-07 |
| TNFa/IFNb-IFNb/IL1b | 1424 | 738.11 | 2109 | 2.45E-05 | 906.3 | -399.8 | 2212 | 0.317382 | -727 | -963 | -491 | 6.33E-08 | -511.62 | -1010.8 | -12.427 | 0.042191 |
| TNFa/IL1b-IFNb/IL1b | 198.1 | -487.4 | 883.6 | 0.972061 | 81.72 | -1224 | 1388 | 0.999999 | -1264 | -1500 | -1028 | 4.16E-12 | -1119.7 | -1618.9 | -620.48 | 8.31E-06 |
| TNFa/IL1b/IFNb-IFNb/IL1b | 1119 | 433.6 | 1805 | 0.000531 | 1520 | 213.57 | 2826 | 0.015933 | 1484 | 1248 | 1720 | 2.23E-13 | 1134.1 | 634.89 | 1633.3 | 6.92E-06 |
| null-IL1b | -775 | -1368 | -181 | 0.005743 | -524 | -1656 | 606.8 | 0.760523 | -396 | -600 | -192 | 6.24E-05 | -279.7 | -712.02 | 152.61 | 0.397257 |
| TNFa-IL1b | 428.7 | -256.9 | 1114 | 0.437538 | 308.9 | -997.3 | 1615 | 0.990936 | -142 | -377 | 94.28 | 0.486079 | 81.797 | -417.4 | 580.99 | 0.999054 |
| TNFa/IFNb-IL1b | 3590 | 2904.3 | 4275 | 6.46E-12 | 2899 | 1593.3 | 4206 | 9.64E-06 | 1287 | 1051 | 1523 | 2.92E-12 | 1064.2 | 564.97 | 1563.4 | 1.71E-05 |
| TNFa/IL1b-IL1b | 2364 | 1678.8 | 3050 | 9.89E-09 | 2075 | 768.72 | 3381 | 0.000728 | 750.5 | 514.6 | 986.4 | 3.77E-08 | 456.11 | -43.083 | 955.3 | 0.08857 |
| TNFa/IL1b/IFNb-IL1b | 3285 | 2599.8 | 3971 | 3.42E-11 | 3513 | 2206.7 | 4819 | 5.51E-07 | 3498 | 3262 | 3734 | 0 | 2709.9 | 2210.7 | 3209.1 | 3.23E-12 |
| TNFa-null | 1203 | 609.48 | 1797 | 3.43E-05 | 833.3 | -297.9 | 1964 | 0.254232 | 254.3 | 50.01 | 458.6 | 0.008869 | 361.5 | -70.816 | 793.81 | 0.143841 |
| TNFa/IFNb-null | 4364 | 3770.7 | 4958 | 0 | 3424 | 2292.7 | 4555 | 8.48E-08 | 1683 | 1479 | 1887 | 0 | 1343.9 | 911.55 | 1776.2 | 5.51E-08 |
| TNFa/IL1b-null | 3139 | 2545.1 | 3732 | 5.38E-12 | 2599 | 1468.1 | 3730 | 5.86E-06 | 1146 | 942.1 | 1351 | 1.72E-12 | 735.81 | 303.5 | 1168.1 | 0.000323 |
| TNFa/IL1b/IFNb-null | 4060 | 3466.2 | 4654 | 4.31E-14 | 4037 | 2906.1 | 5168 | 5.56E-09 | 3894 | 3690 | 4098 | 0 | 2989.6 | 2557.3 | 3421.9 | 3.20E-14 |
| TNFa/IFNb-TNFa | 3161 | 2475.7 | 3847 | 6.84E-11 | 2591 | 1284.4 | 3897 | 4.59E-05 | 1429 | 1193 | 1665 | 4.29E-13 | 982.37 | 483.17 | 1481.6 | 5.09E-05 |
| TNFa/IL1b-TNFa | 1936 | 1250.1 | 2621 | 2.57E-07 | 1766 | 459.83 | 3072 | 0.004063 | 892.1 | 656.2 | 1128 | 2.08E-09 | 374.31 | -124.88 | 873.51 | 0.236722 |
| TNFa/IL1b/IFNb-TNFa | 2857 | 2171.2 | 3542 | 3.97E-10 | 3204 | 1897.8 | 4510 | 2.24E-06 | 3640 | 3404 | 3875 | 0 | 2628.1 | 2128.9 | 3127.3 | 5.84E-12 |
| TNFa/IL1b-TNFa/IFNb | -1226 | -1911 | -540 | 0.000176 | -825 | -2131 | 481.6 | 0.426185 | -537 | -773 | -301 | 6.74E-06 | -608.05 | -1107.2 | -108.86 | 0.010761 |
| TNFa/IL1b/IFNb-TNFa/IFNb | -305 | -990 | 381 | 0.795358 | 613.4 | -692.8 | 1920 | 0.749257 | 2211 | 1975 | 2447 | 0 | 1645.7 | 1146.5 | 2144.9 | 2.10E-08 |
| TNFa/IL1b/IFNb-TNFa/IL1b | 921 | 235.51 | 1607 | 0.004323 | 1438 | 131.84 | 2744 | 0.024853 | 2747 | 2512 | 2983 | 0 | 2253.8 | 1754.6 | 2752.9 | 9.94E-11 |

**Table S2: Pair wise comparisons for CD86 of DCs treated in all combinations with IFNβ, TNFα and IL1b.** Pair wise comparisons were calculated with ANOVA followed by Tukey's 'Honest Significant Difference' method.

| | HLA-DR 1:1 | | | | HLA-DR 1:2 | | | | HLA-DR 1:4 | | | | HLA-DR 1:8 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Comparisons | diff | lwr | upr | p adj | diff | lwr | upr | p adj | diff | lwr | upr | p adj | diff | lwr | upr | p adj |
| IFNb/IL1b-IFNb | 4589 | -2547 | 11725 | 0.40441 | 4279 | -2652 | 11209 | 0.452785 | 4255 | 2500 | 6011 | 2.67E-06 | 2574.6 | 29.2 | 5120.1 | 0.046248 |
| IL1b-IFNb | 1478 | -5659 | 8614 | 0.995899 | 865 | -6065 | 7796 | 0.999841 | 707 | -1049 | 2462 | 0.861868 | 602.3 | -1943.1 | 3147.8 | 0.990902 |
| null-IFNb | -2900 | -9080 | 3280 | 0.749974 | -2968 | -8970 | 3034 | 0.701285 | -3058 | -4578 | -1537 | 3.80E-05 | -2936.0 | -5140.4 | -731.6 | 0.004708 |
| TNFa-IFNb | 5854 | -1283 | 12990 | 0.158249 | 2887 | -4043 | 9818 | 0.840835 | -474 | -2230 | 1281 | 0.980642 | 309.4 | -2236.0 | 2854.8 | 0.999866 |
| TNFa/IFNb-IFNb | 7076 | -60 | 14213 | 0.052935 | 5927 | -1004 | 12858 | 0.128117 | 1392 | -363 | 3148 | 0.185472 | 523.8 | -2021.7 | 3069.2 | 0.996056 |
| TNFa/IL1b-IFNb | 13705 | 6568 | 20841 | 7.04E-05 | 12030 | 5099 | 18960 | 0.000254 | 6190 | 4435 | 7946 | 6.82E-09 | 3509.1 | 963.6 | 6054.5 | 0.003348 |
| TNFa/IL1b/IFNb-IFNb | 10281 | 3145 | 17418 | 0.002128 | 11647 | 4716 | 18577 | 0.000377 | 10675 | 8920 | 12430 | 4.02E-13 | 7832.5 | 5287.1 | 10378.0 | 6.50E-08 |
| IL1b-IFNb/IL1b | -3111 | -10248 | 4025 | 0.809459 | -3413 | -10344 | 3517 | 0.705152 | -3549 | -5304 | -1793 | 3.55E-05 | -1972.3 | -4517.7 | 573.1 | 0.20601 |
| null-IFNb/IL1b | -7489 | -13669 | -1309 | 0.011261 | -7246 | -13248 | -1244 | 0.011632 | -7313 | -8833 | -5793 | 3.20E-11 | -5510.6 | -7715.0 | -3306.2 | 1.69E-06 |
| TNFa-IFNb/IL1b | 1265 | -5872 | 8401 | 0.998442 | -1391 | -8322 | 5540 | 0.996612 | -4730 | -6485 | -2974 | 5.36E-07 | -2265.2 | -4810.7 | 280.2 | 0.103112 |
| TNFa/IFNb-IFNb/IL1b | 2487 | -4649 | 9623 | 0.927716 | 1648 | -5282 | 8579 | 0.99063 | -2863 | -4618 | -1108 | 0.000537 | -2050.9 | -4596.3 | 494.6 | 0.172477 |
| TNFa/IL1b-IFNb/IL1b | 9116 | 1979 | 16252 | 0.007003 | 7751 | 820 | 14682 | 0.021971 | 1935 | 179 | 3690 | 0.024654 | 934.4 | -1611.0 | 3479.9 | 0.907876 |
| TNFa/IL1b/IFNb-IFNb/IL1b | 5692 | -1444 | 12828 | 0.180809 | 7368 | 438 | 14299 | 0.032391 | 6420 | 4664 | 8175 | 3.68E-09 | 5257.9 | 2712.4 | 7803.3 | 2.64E-05 |
| null-IL1b | -4378 | -10558 | 1802 | 0.294912 | -3833 | -9835 | 2169 | 0.412601 | -3764 | -5285 | -2244 | 1.95E-06 | -3538.3 | -5742.7 | -1333.9 | 0.000646 |
| TNFa-IL1b | 4376 | -2760 | 11512 | 0.460796 | 2022 | -4908 | 8953 | 0.970581 | -1181 | -2936 | 575 | 0.352093 | -292.9 | -2838.4 | 2252.5 | 0.999907 |
| TNFa/IFNb-IL1b | 5598 | -1538 | 12735 | 0.195019 | 5062 | -1869 | 11992 | 0.262963 | 686 | -1070 | 2441 | 0.878488 | -78.6 | -2624.0 | 2466.9 | 1 |
| TNFa/IL1b-IL1b | 12227 | 5090 | 19363 | 0.000298 | 11165 | 4234 | 18095 | 0.00062 | 5483 | 3728 | 7239 | 5.09E-08 | 2906.7 | 361.3 | 5452.2 | 0.018587 |
| TNFa/IL1b/IFNb-IL1b | 8803 | 1667 | 15940 | 0.009619 | 10782 | 3851 | 17712 | 0.000923 | 9968 | 8213 | 11724 | 1.38E-12 | 7230.2 | 4684.7 | 9775.6 | 2.34E-07 |
| TNFa-null | 8754 | 2574 | 14934 | 0.00254 | 5855 | -147 | 11857 | 0.058972 | 2583 | 1063 | 4104 | 0.00033 | 3245.4 | 1041.0 | 5449.8 | 0.001691 |
| TNFa/IFNb-null | 9976 | 3796 | 16157 | 0.000605 | 8895 | 2893 | 14897 | 0.001576 | 4450 | 2930 | 5970 | 1.45E-07 | 3459.8 | 1255.3 | 5664.2 | 0.000835 |
| TNFa/IL1b-null | 16605 | 10424 | 22785 | 5.60E-07 | 14997 | 8995 | 21000 | 1.70E-06 | 9248 | 7727 | 10768 | 3.99E-13 | 6445.0 | 4240.6 | 8649.5 | 1.48E-07 |
| TNFa/IL1b/IFNb-null | 13181 | 7001 | 19361 | 1.70E-05 | 14615 | 8612 | 20617 | 2.50E-06 | 13733 | 12212 | 15253 | 0.00 | 10768.5 | 8564.1 | 12972.9 | 2.41E-11 |
| TNFa/IFNb-TNFa | 1222 | -5914 | 8359 | 0.998744 | 3039 | -3891 | 9970 | 0.80508 | 1867 | 111 | 3622 | 0.032335 | 214.4 | -2331.1 | 2759.8 | 0.999989 |
| TNFa/IL1b-TNFa | 7851 | 714 | 14987 | 0.024997 | 9142 | 2212 | 16073 | 0.005167 | 6664 | 4909 | 8420 | 1.95E-09 | 3199.6 | 654.2 | 5745.1 | 0.008117 |
| TNFa/IL1b/IFNb-TNFa | 4427 | -2709 | 11564 | 0.446906 | 8759 | 1829 | 15690 | 0.007724 | 11149 | 9394 | 12905 | 1.89E-13 | 7523.1 | 4977.7 | 10068.5 | 1.24E-07 |
| TNFa/IL1b-TNFa/IFNb | 6628 | -508 | 13765 | 0.080292 | 6103 | -828 | 13034 | 0.109391 | 4798 | 3042 | 6553 | 4.29E-07 | 2985.3 | 439.8 | 5530.7 | 0.014907 |
| TNFa/IL1b/IFNb-TNFa/IFNb | 3205 | -3931 | 10341 | 0.786751 | 5720 | -1211 | 12651 | 0.15358 | 9283 | 7527 | 11038 | 5.36E-12 | 7308.7 | 4763.3 | 9854.2 | 1.97E-07 |
| TNFa/IL1b/IFNb-TNFa/IL1b | -3424 | -10560 | 3713 | 0.730042 | -383 | -7314 | 6548 | 0.999999 | 4485 | 2729 | 6240 | 1.21E-06 | 4323.5 | 1778.0 | 6868.9 | 0.000331 |

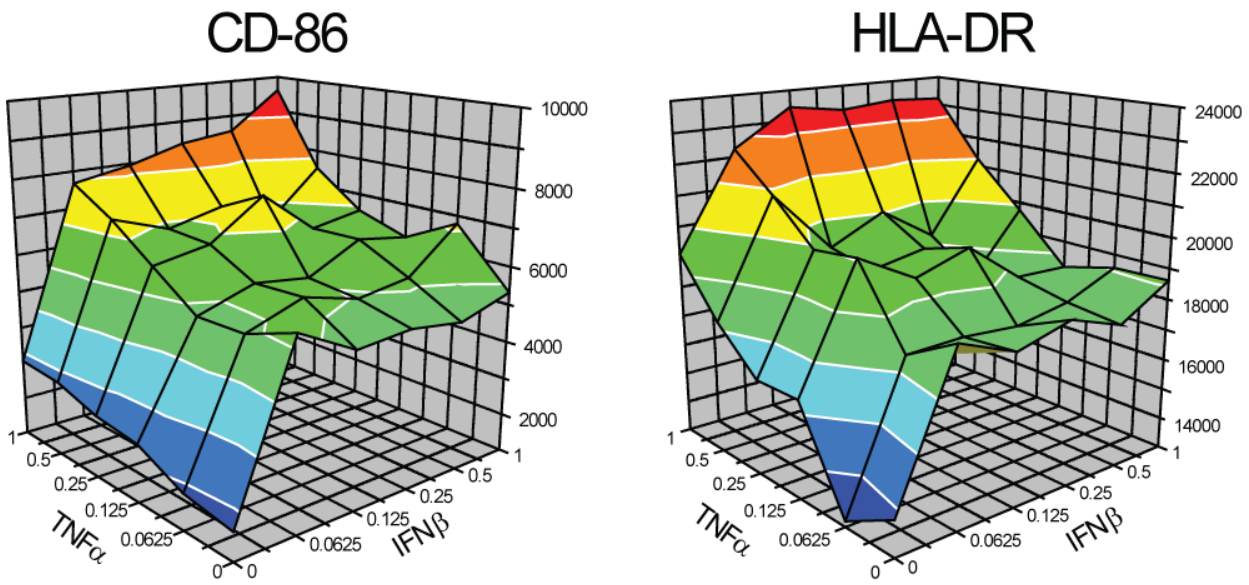


**Figure S3: Combinatorial effects of IFNβ and TNFα on DC maturation marker expression.** DCs were exposed to all possible combinations of dilutions of IFNβ and TNFα for 8 hours. Maturation marker expression was measured by flow cytometry

**Table S3: Table with primers used in analysis**

| GENE | Sense | Antisense |
|---|---|---|
| CXCL1 | CACTGCGCCCAAACCGAAGT | TCCCTTCTGGTCAGTTGGAT |
| IL28 | GCCTTTAAGAGGGCCAAAGA | GAGGATATGGTGCAGGGTGT |
| TNFSF4 | CATGGTCCCCTCTCTTAGGT | TGGAGTGAGGCTGGTGCATA |
| TNFSF15 | GGGTTGGAGGATTGGCGAGT | CTGGACCACTGGTGACCATT |
| IL29 | GCCTCCTCACGCGAGACCTC | GGAGTAGGGCTCAGCGCATA |
| IL18 | GAGGATGATGAATTGGGGGATAG | TAGCTGGGATTGAGGGCATG |
| IFNa16 | GGTGTTTGATGGCAACCAGT | GTCACACAGGCTTCTAGGTC |
| VCAM1 | TCAGATTGGTGACTCCGTCT | TCACCTTCCCATTCAGTGGA |
| CCL3L1 | GTGCTCCAAGCCCAGTGTCA | TCTGGACCCCTCAGGCACTC |
| CCL3L3 | GTGCTCCAAGCCCAGTGTCA | AGGTCACACGCATGTTCCCA |
| AQP9 | AGAGAAGCCCCAAGATGCAG | CACAGCCACATCCAAGGACA |
| CSF1 | ACCCGCAGACCCTTGACTGA | TCACCAGCCTTCCTCAAGCA |
| RIPK2 | CCAAGCCTACAAGGACCTCA | GGTAAGGCTGAAGACCCATT |
| CST7 | TGTTCAAGGAGTCCCGCATC | ACAGTCATCCAGACGCAGGT |
| CD40 | AGAACCTCTCACTTCACCCT | ACCAAACTGCTGGATCGGAA |
| EDN | CAGCAGAAACACACAGTCACA | ACACTCCCTTAGGACCTTCGT |
| CLECA5A | GAGATCAGCAGAGCCACCCTA | GCCAGATGGAGATTGCATCAGT |
| CD274 | GCCAGAAAAGCCTCATTCGT | CCCAGGGCATCTGAATCTCG |
| IL7R | GGACCTCCTGCTTAGCCTT | TCATCTTTGTCGCTCACGGTA |
| OSM | GCCTCATCATGTCCCAAACC | ATCCAAGCAACCGACAGGCA |
| IRAK2 | AGTCACTGCCTGGTACCTT | CAGGTGCCTACAGTCCCAT |
| IL6 | AATGCCAGCCTGCTGACGAA | CTGAGGTGCCCATGCTACAT |
| PTGER4 | ATTCGTCCGCCTCCTTGAGC | ACAGCCAGCCCACATACCAG |