Supplementary Tables

Supplementary Table S1. Expression of kinases and DUSPs (z-scores) in hematopoietic cells (matrix from Rieckmann et al, Nat Immunol (2017))

Supplementary Table S2. Matrix for corresponding RNA and protein expression data (z-scores) for T4 naïve, T4 TCM, B memory and classical monocyte cells

Supplementary Table S3. Expression of DUSPs and protein kinases in primary and secondary lymphoid tissue expression datasets.

Supplementary Table S4. Correlation matrix between DUSP and protein kinase expression in hematopoietic cells (data from Rieckmann et al, Nat Immunol (2017)). Spearman's rank correlation coefficient was used.

Supplementary Table S5. List of nodes and their properties from the comPPI interactome for DUSP family members. The interactions were obtained from the comPPI database and the network properties analyzed using Network Analyzer in Cytoscape.

Supplementary Table S6. Expression of kinases and DUSPs in activated hematopoietic cells (matrix from Rieckmann et al, Nat Immunol (2017)). Ratios obtained by dividing expression values in the activated state by expression values in the steady-state.

Supplementary Table S7. log2(fold-change) of kinases and DUSPs in LPS-stimulated hematopoietic cells. Ratios obtained by dividing expression values in the activated state by expression values in the steady-state and log transformation to the base 2. The study code indicated in the header can be referred to in Supplementary Table 1. The kind of biomolecule assayed and the time point after LPS stimulation is mentioned in the header.

Supplementary Table S8. List of DUSPs and kinases differentially expressed in monocytes and dendritic cells in response to LPS

Supplementary Table S9. List of enriched pathways containing proteins differentially expressed in monocytes and dendritic cells in response to LPS

Supplementary Table S10. Correlation matrix between DUSP and protein kinase expression in activated DCs and MOs. Spearman's rank correlation coefficient was used.

Supplementary Table S11. List of datasets used for the study

Supplementary Table S12. List of DUSP family genes used for the study and their details

Supplementary Table S13. List of protein kinases used for the study and their details

Supplementary Figures

Supplementary Figure 1. Baseline expression of A.DUSPs and B. protein kinases in hematopoietic cell line proteomic data. The raw hematopoietic cell expression data obtained from Rieckmann *et al*, *Nat Immunol* (2017) was scaled to obtain Z-scores. Z-scores were plotted as a heatmap using Morpheus and hierarchical clustering was carried out using Euclidean distance, complete linkage by both rows and columns. TUBB gene, observed to occur consistently across all cell types, was added to the heatmaps for comparison purpose

Supplementary Figure 2. DUSP interaction network. Protein-protein interaction data between DUSP and other proteins were obtained from Compartmentalized Protein-Protein Interaction (comPPI) Database were analyzed in Cytoscape using Network Analyzer to obtain network properties including Betweenness Centrality. Proteins with high Betweenness Centrality indicate primary regulatory proteins associated with DUSPs. Manual clustering of proteins within the vicinity of DUSPs was carried out using AutoAnnotate 1.3 in Cytoscape.

Supplementary Figure 3. (a) Differential expression of DUSPs in various activated hematopoietic cells. (b). Differential expression of protein kinases in various activated hematopoietic cells.

Supplementary Figure 4. Expression of (a) DUSPs and (b) protein kinases in activated hematopoietic cells. Expression ratios from activated and steady-state hematopoietic cells were calculated from expression data obtained from Rieckmann *et al, Nat Immunol* (2017) and log transformed. Expression values were plotted as a heatmap using Morpheus and hierarchical clustered by Euclidean distance and complete linkage by both rows and columns. **Similarity matrices for (c) DUSP and (d) protein kinase expression in hematopoietic cells.** DUSP and protein kinase expression in various cell types was correlated via Spearman's rank correlation.

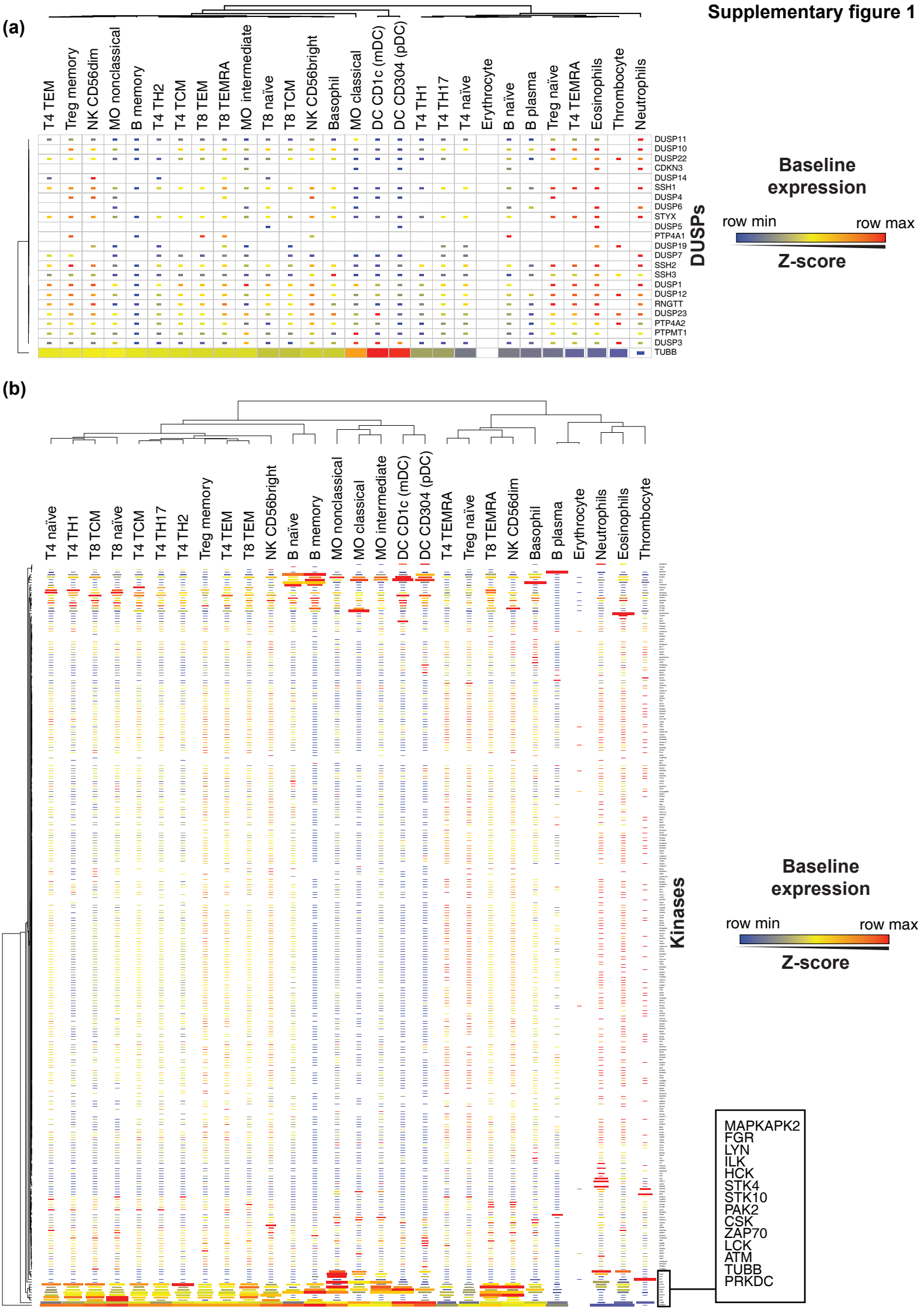
Supplementary Figure 5: Venn diagrams showing the overlap of molecules differentially expressed in response to LPS in **(a).** murine and human dendritic cells (DCs). **(b)**. human dendritic cells and monocytes (upregulated molecules). **(c)** human dendritic cells and monocytes (downregulated molecules). **(d) Correlation of protein kinase and DUSP expression patterns in activated DCs and MOs**. The correlation was carried out using Spearman's rank correlation method to identify kinase-DUSP pairs that may have reciprocal activities.

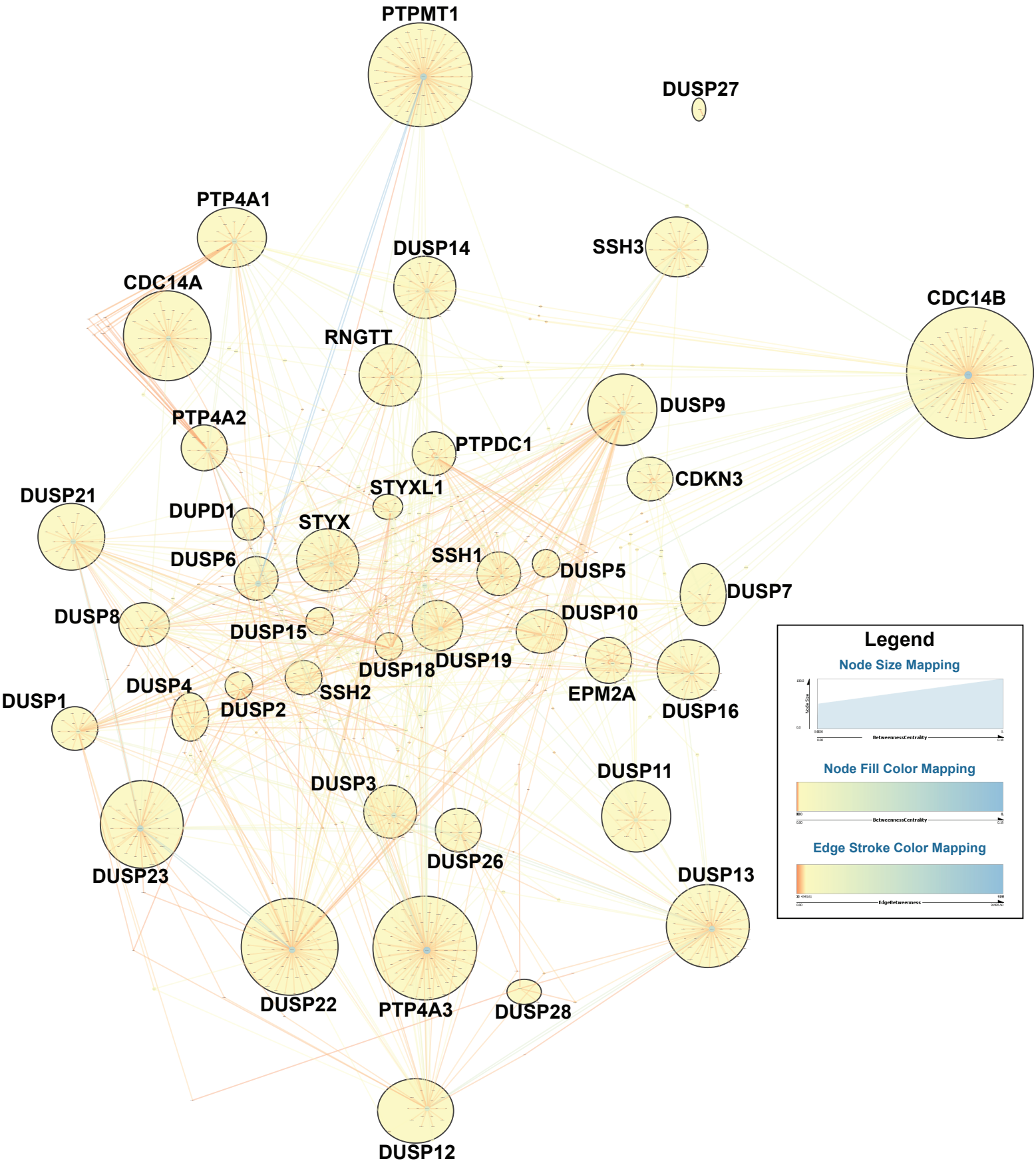
Supplementary Figure 6. Network analysis of DUSPs and kinases that were (a). upregulated and (b). downregulated in activated murine dendritic cells

Supplementary Figure 7: Network analysis of DUSPs and kinases that were (a). upregulated and (b) downregulated in activated human dendritic cells

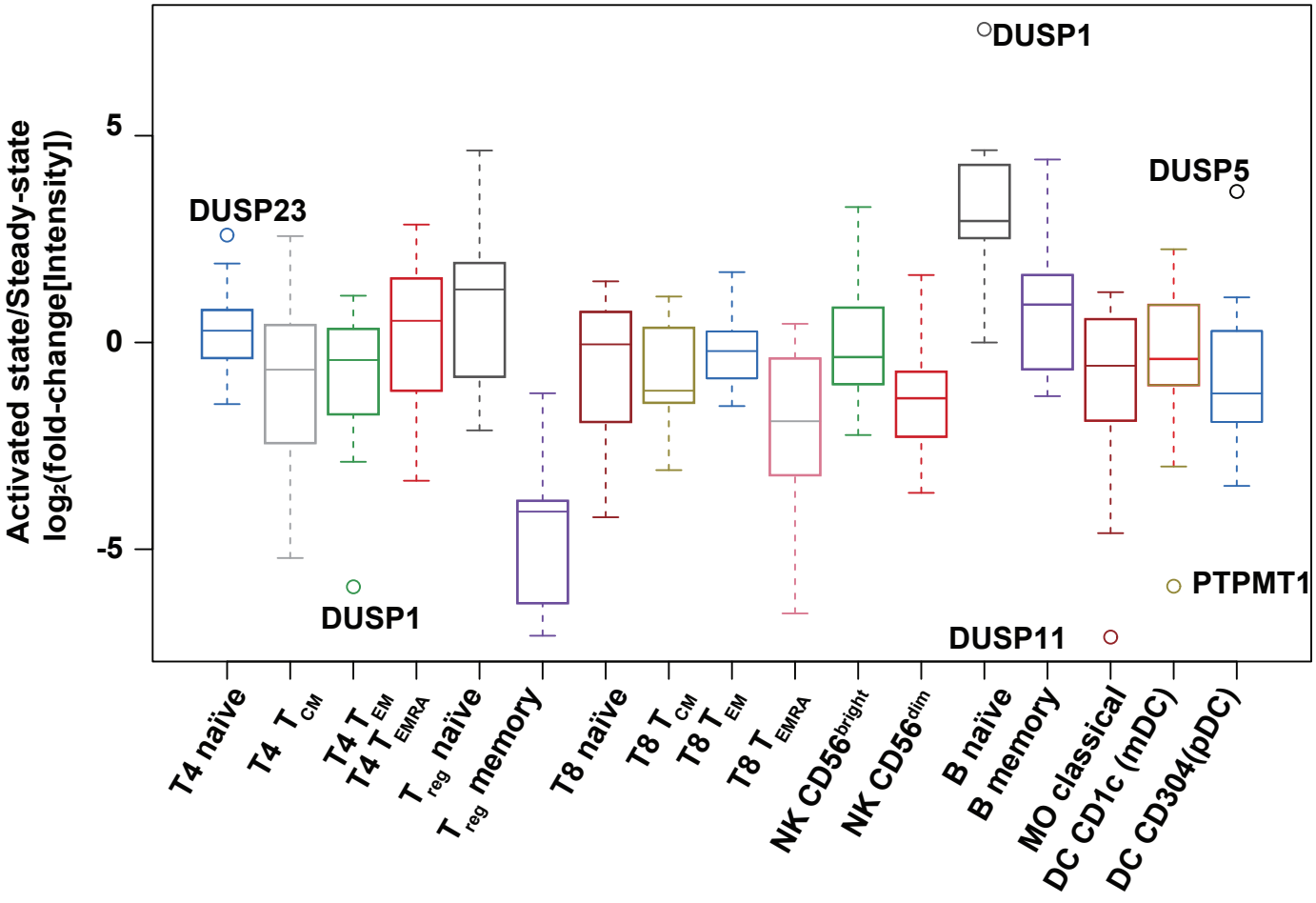
Supplementary Figure 8: Network analysis of DUSPs and kinases that were (a). upregulated and (b) downregulated in activated human monocytes

Supplementary figure 1

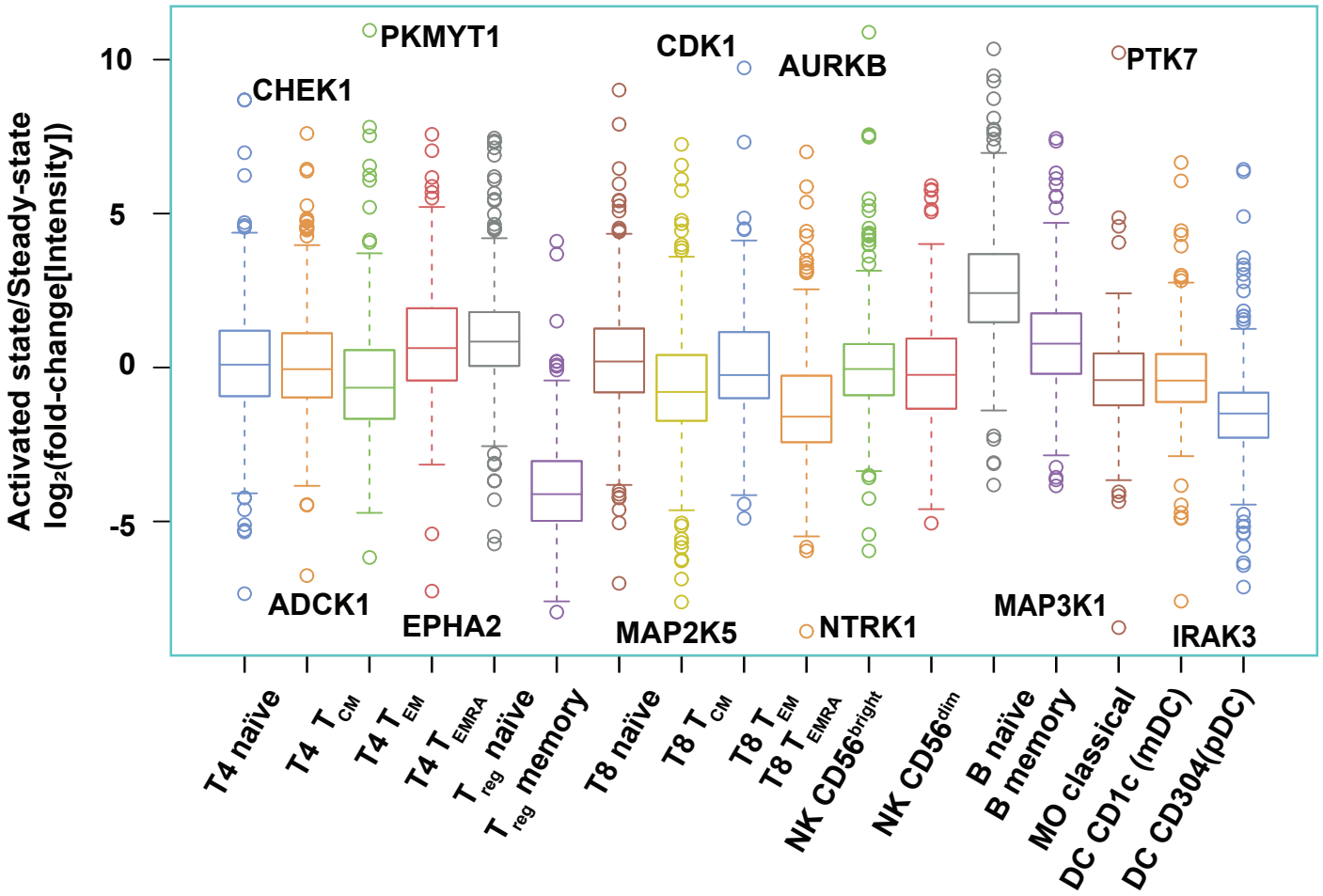


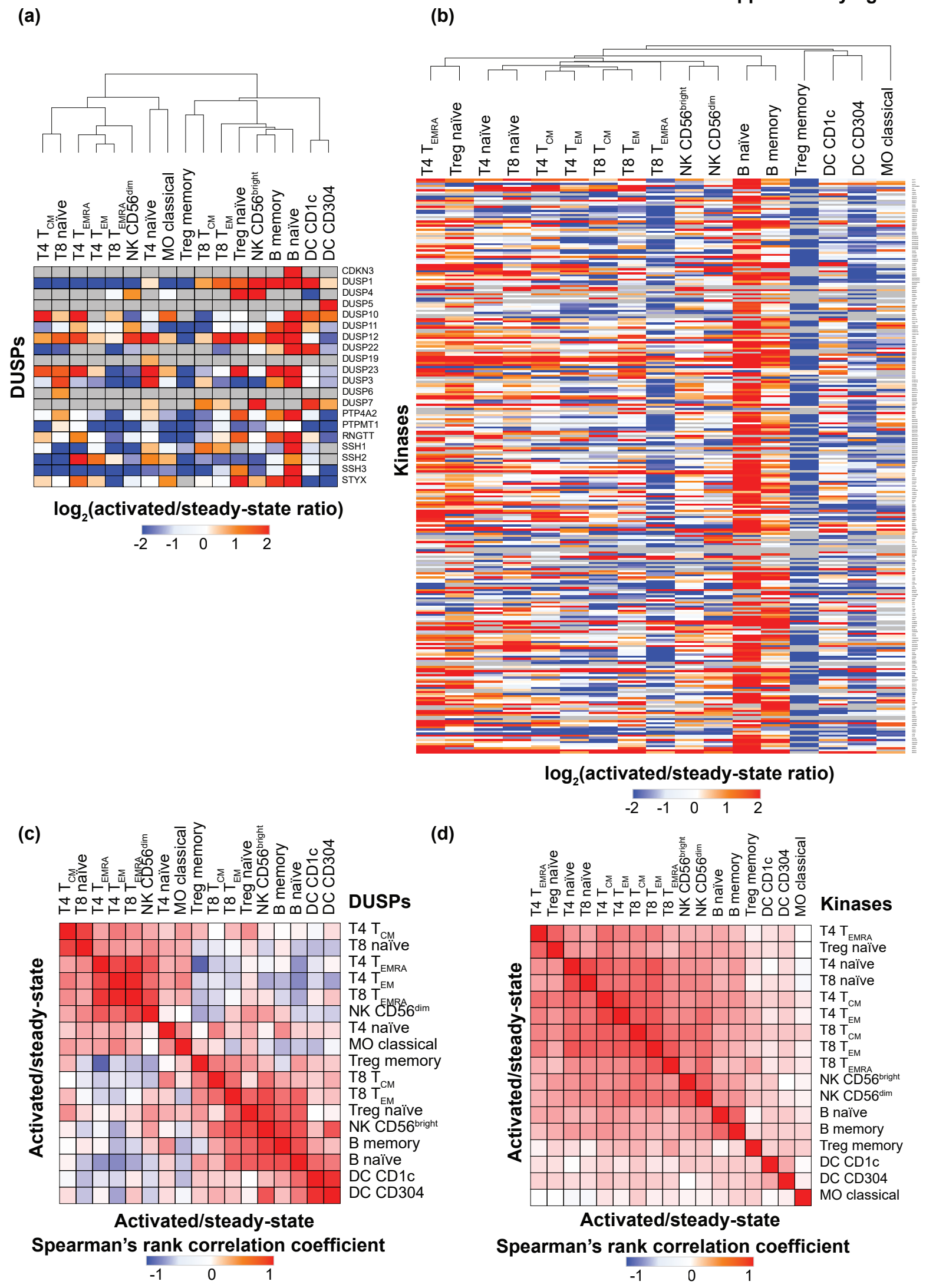

PTPMT1
DUSP27
PTP4A1
DUSP14
SSH3
CDC14A
CDC14B
RNGTT
DUSP9
PTP4A2
PTPDC1
CDKN3
STYXL1
DUSP21
DUPD1
STYX
DUSP6
SSH1
DUSP5
DUSP7
DUSP8
DUSP15
DUSP10
DUSP18
DUSP19
DUSP4
SSH2
EPM2A
DUSP16
DUSP1
DUSP2
DUSP3
DUSP11
DUSP23
DUSP26
DUSP13
DUSP22
PTP4A3
DUSP28
DUSP12
Legend
Node Size Mapping
BetweennessCentrality
Node Fill Color Mapping
BetweennessCentrality
Edge Stroke Color Mapping
EdgeBetweenness

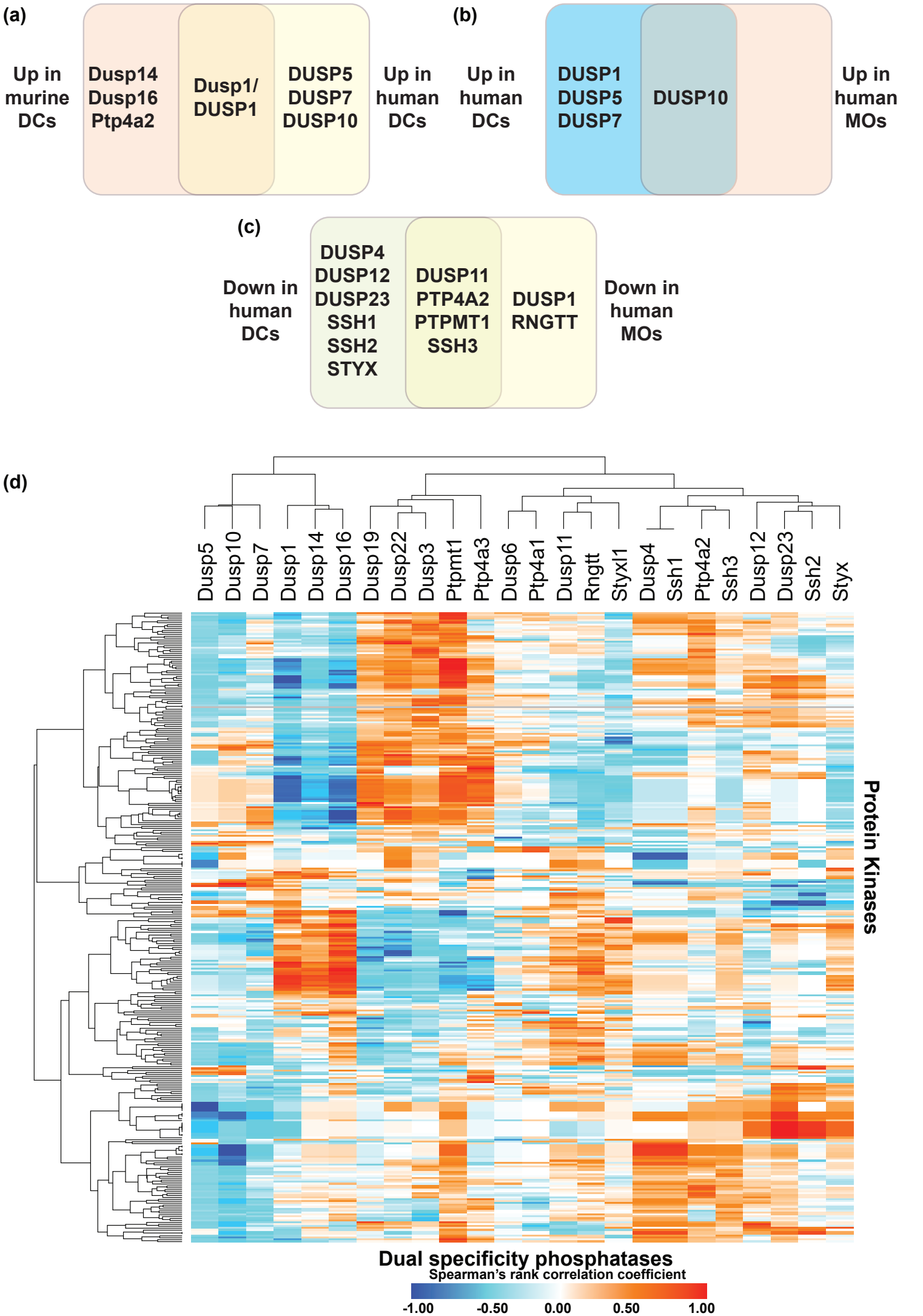
(a)

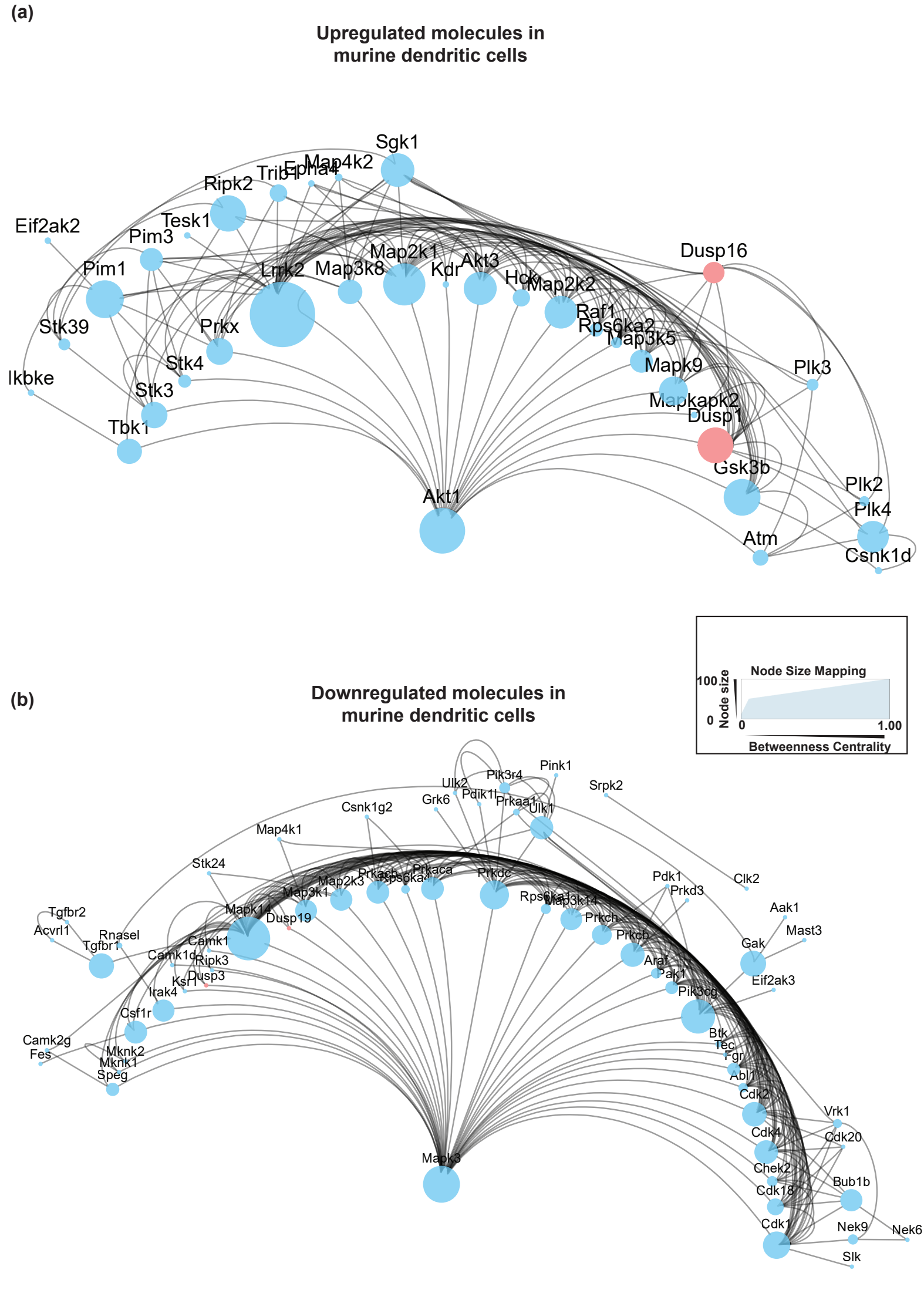

Activated state/Steady-state
log2(fold-change[Intensity])
5
0
-5
DUSP1
DUSP5
DUSP23
DUSP1
PTPMT1
DUSP11
T4 naive
T4 TCM
T4 TEM
T4 TEMRA
Treg naive
Treg memory
T8 naive
T8 TCM
T8 TEM
T8 TEMRA
NK CD56bright
NK CD56dim
B naive
B memory
MO classical
DC CD1c (mDC)
DC CD304(pDC)

(b)


Activated state/Steady-state
log2(fold-change[Intensity])
10
5
0
-5
PKMYT1
CDK1
AURKB
PTK7
CHEK1
ADCK1
EPHA2
MAP2K5
NTRK1
MAP3K1
IRAK3
T4 naive
T4 TCM
T4 TEM
T4 TEMRA
Treg naive
Treg memory
T8 naive
T8 TCM
T8 TEM
T8 TEMRA
NK CD56bright
NK CD56dim
B naive
B memory
MO classical
DC CD1c (mDC)
DC CD304(pDC)


(a)
T4 T CM
T8 naïve
T4 T EMRA
T4 T EM
T8 T EMRA
NK CD56dim
T4 naïve
MO classical
Treg memory
T8 T CM
T8 T EM
Treg naïve
NK CD56bright
B memory
B naïve
DC CD1c
DC CD304
DUSPs
CDKN3
DUSP1
DUSP4
DUSP5
DUSP10
DUSP11
DUSP12
DUSP22
DUSP19
DUSP23
DUSP3
DUSP6
DUSP7
PTP4A2
PTPMT1
RNGTT
SSH1
SSH2
SSH3
STYX
log2(activated/steady-state ratio)
-2 -1 0 1 2
(b)
T4 T EMRA
Treg naïve
T4 naïve
T8 naïve
T4 T CM
T4 T EM
T8 T CM
T8 T EM
T8 T EMRA
NK CD56bright
NK CD56dim
B naïve
B memory
Treg memory
DC CD1c
DC CD304
MO classical
Kinases
log2(activated/steady-state ratio)
-2 -1 0 1 2
(c)
DUSPs
Activated/steady-state
Activated/steady-state
Spearman's rank correlation coefficient
-1 0 1
(d)
Kinases
Activated/steady-state
Activated/steady-state
Spearman's rank correlation coefficient
-1 0 1

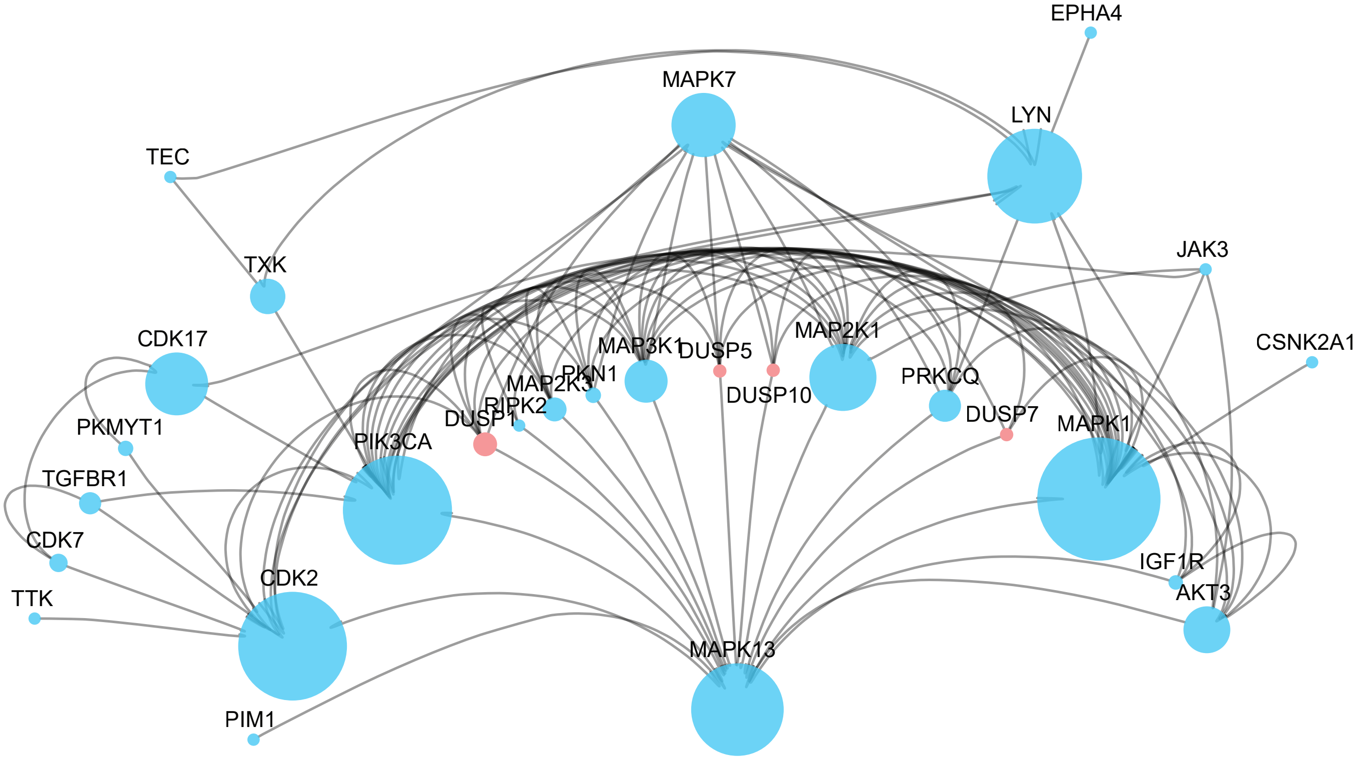

(a)
Up in murine DCs
Dusp14
Dusp16
Ptp4a2
Dusp1/ DUSP1
DUSP5
DUSP7
DUSP10
Up in human DCs
(b)
Up in human DCs
DUSP1
DUSP5
DUSP7
DUSP10
Up in human MOs
(c)
Down in human DCs
DUSP4
DUSP12
DUSP23
SSH1
SSH2
STYX
DUSP11
PTP4A2
PTPMT1
SSH3
DUSP1
RNGTT
Down in human MOs
(d)
Dusp5
Dusp10
Dusp7
Dusp1
Dusp14
Dusp16
Dusp19
Dusp22
Dusp3
Ptpmt1
Ptp4a3
Dusp6
Ptp4a1
Dusp11
Rngtt
Styxl1
Dusp4
Ssh1
Ptp4a2
Ssh3
Dusp12
Dusp23
Ssh2
Styx
Protein Kinases
Dual specificity phosphatases
Spearman's rank correlation coefficient
-1.00
-0.50
0.00
0.50
1.00

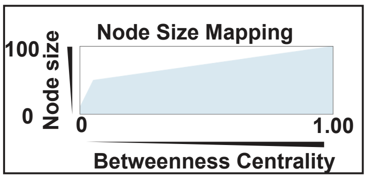

(a)
Upregulated molecules in murine dendritic cells
Sgk1
Map4k2
Epha4
Trib1
Ripk2
Tesk1
Eif2ak2
Pim3
Pim1
Lrrk2
Map3k8
Map2k1
Kdr
Akt3
Hck
Map2k2
Dusp16
Raf1
Rps6ka2
Map3k5
Stk39
Prkx
Stk4
Mapk9
Plk3
Ikbke
Stk3
Mapkapk2
Tbk1
Dusp1
Gsk3b
Plk2
Plk4
Akt1
Atm
Csnk1d
Node Size Mapping
100
Node size
0
0
1.00
Betweenness Centrality
(b)
Downregulated molecules in murine dendritic cells
Pink1
Pik3r4
Ulk2
Srpk2
Pdik1l
Grk6
Prkaa1
Csnk1g2
Ulk1
Map4k1
Stk24
Prkaca
Prkdc
Map2k3
Pdk1
Clk2
Map3k1
Prkd3
Rps6ka1
Map3k14
Tgfbr2
Mapk14
Dusp19
Prkch
Aak1
Acvrl1
Rnasel
Prkcb
Mast3
Tgfbr1
Camk1
Araf
Gak
Camk1d
Ripk3
Pak1
Dusp3
Eif2ak3
Ksr1
Pik3cg
Irak4
Csf1r
Btk
Camk2g
Tec
Fes
Fgr
Mknk2
Abl1
Mknk1
Cdk2
Speg
Vrk1
Cdk4
Cdk20
Mapk3
Chek2
Bub1b
Cdk18
Cdk1
Nek9
Nek6
Slk

Supplementary figure 7

(a)

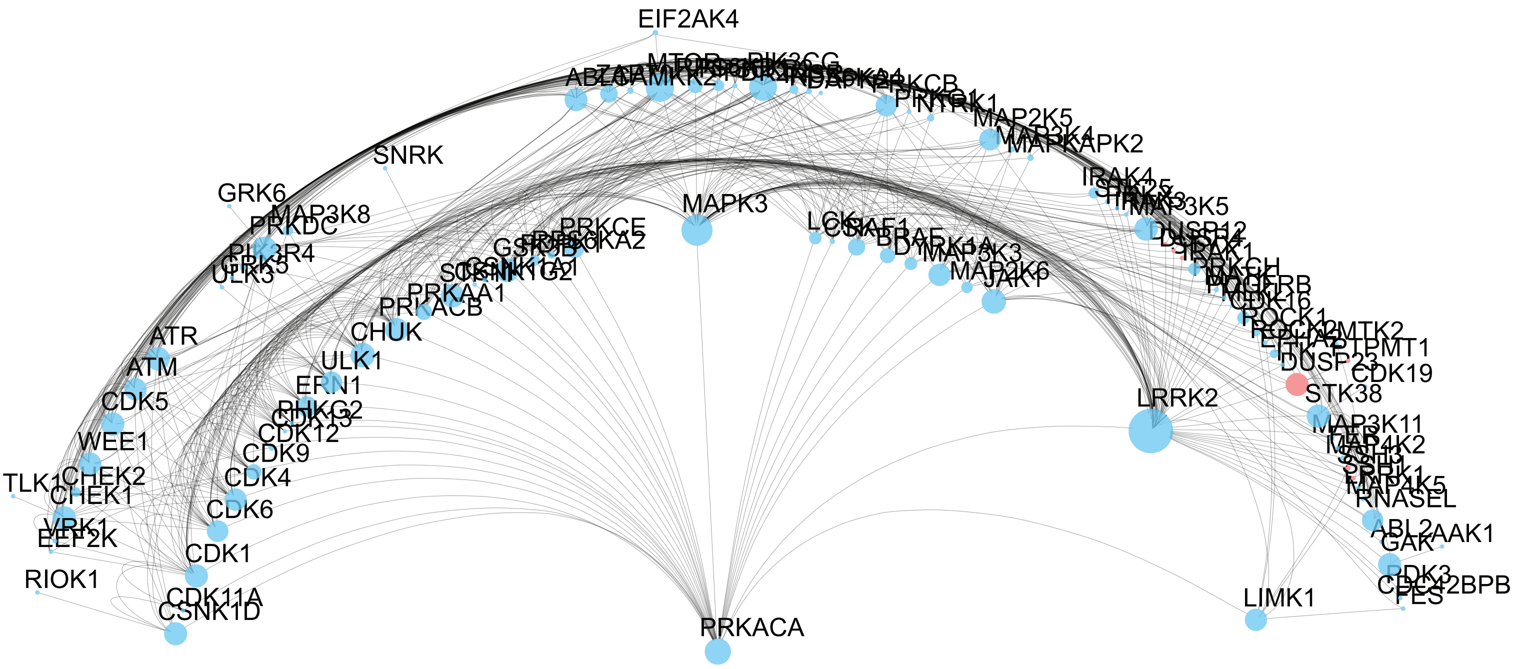
Upregulated molecules in human dendritic cells





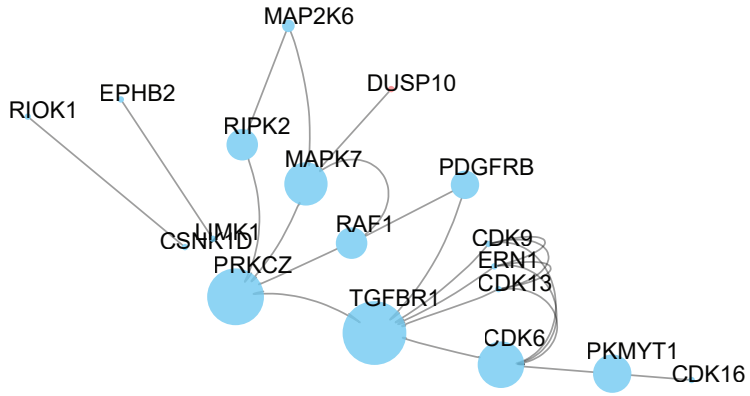
(b)

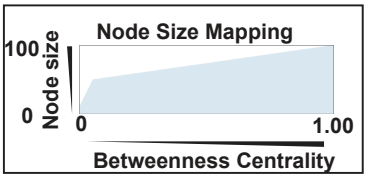
Downregulated molecules in human dendritic cells



(a)

Upregulated molecules in human monocytes





(b)

Downregulated molecules in human monocytes