Correlation Network Analysis of Human Time-courses

- Time-couses of potential interest i.e. include early time points
- Each gene level dataset examined for data quality and evidence of significant time dependent regulation of genes
- 3 inspected in detail (MCF7+EGF1orHRG, MDM+LPS, Lymph endo+VEGF) initially and then a fourth (ARPE-19+TNF)
- Performed iterative cluster analysis of each dataset in order identify IEGs/early response genes
- Results compared across datasets in order to identify common IEGs/early response genes
- Of the 1027 genes called as early regulated in any of the four datsets,
    - **24** shared by all
    - **54** in 3 out 4
    - **152** in 2 out of 4

Common to all four datasets (24)

ATF3
CCRN4L
CSRNP1
DUSP1
DUSP2
EGR1
EGR2
EGR3
EHD1
ETS2
FOS
FOSB
FOSL1
HES1
JUN
JUNB
KLF2
MAFF
NR4A1
PLK3
PPP1R15A
ZC3H12A
ZFP36

Common to three datasets (54)

AKAP2
BMP2
BTG2
C11orf96
CCL20
CCNL1
CDC42EP4
CDK17
CLDN1
CXCL1
CXCL2
CXCL3
DUSP5
DUSP8
ELF4
ERRFI1
FJX1
FOSL2
GADD45B
ID1
IER5
IL6
IRAK2
IRF2BPL
ITPRIP
KDM6B
KLF10
KLF4
KLF6
LIF
MAP2K3
MCL1
MIDN
MIR155HG
NFKBIA
NFKBIZ
NR4A3
PHLDA1
PIM3
PMAIP1
PPP1R15B
RHOB
SDC4
SGK1
SLC25A25
SMOX
SNAI1
SOCS3
SPSB1
TIPARP
TNF
TNFAIP3
TNFAIP8
TRIB1

Observations

- Common core signature, many up-regulated within minutes (peak 45 min - 1h)
- As time continues response diverseifies
- Pattern of regulation varies, many rapid activation and decline, others up-regulated quickly but expression sustained
- There seems to be a correlation between the degree of up-regulation and the subsequent response
- In the main they can be divided into transcription factors, feedback inhibitors, chemoattractants/signalling

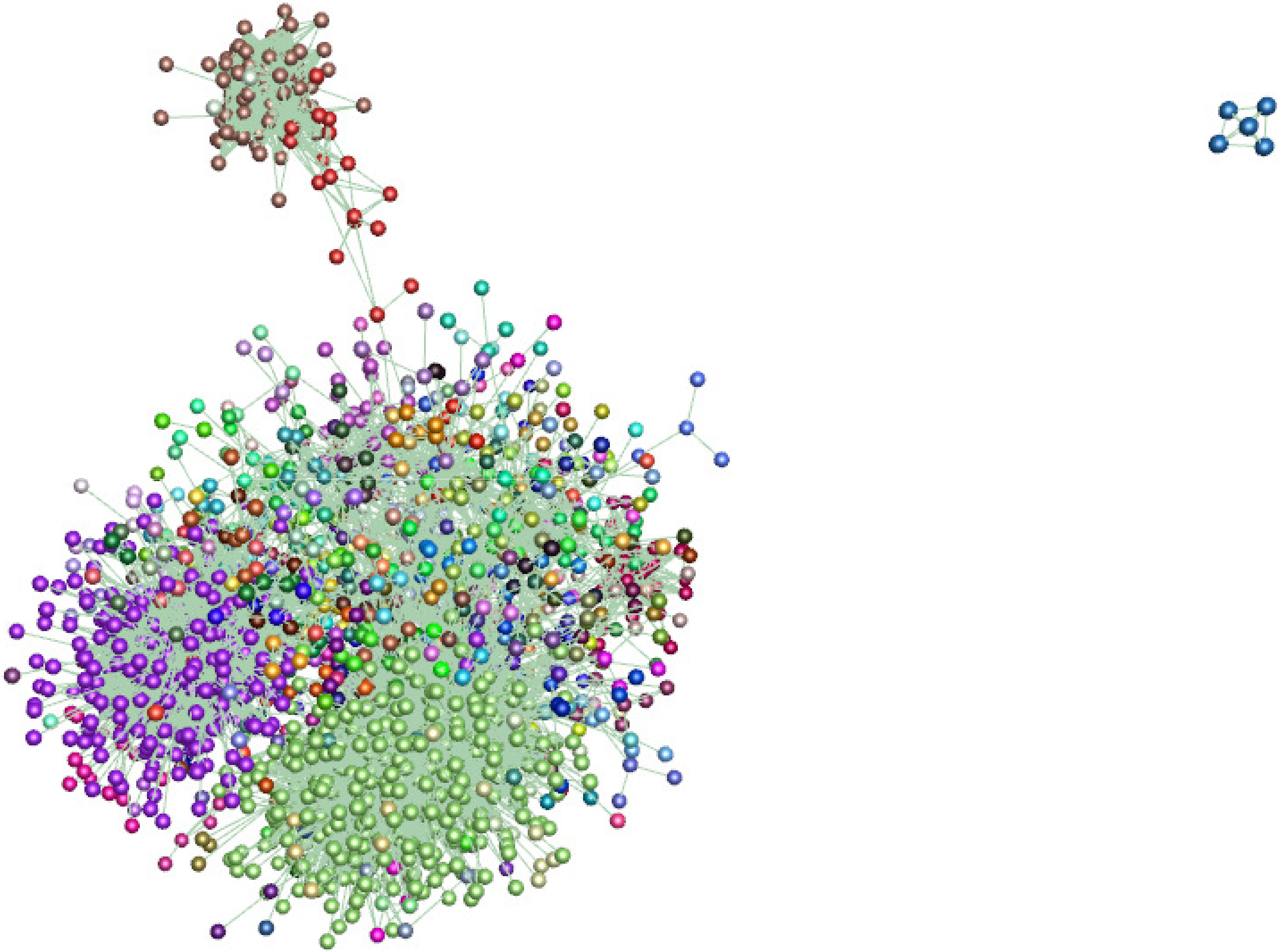
To do

- Expand analysis to promoter level data
- Examine mouse data
- Summarise and categorise genes

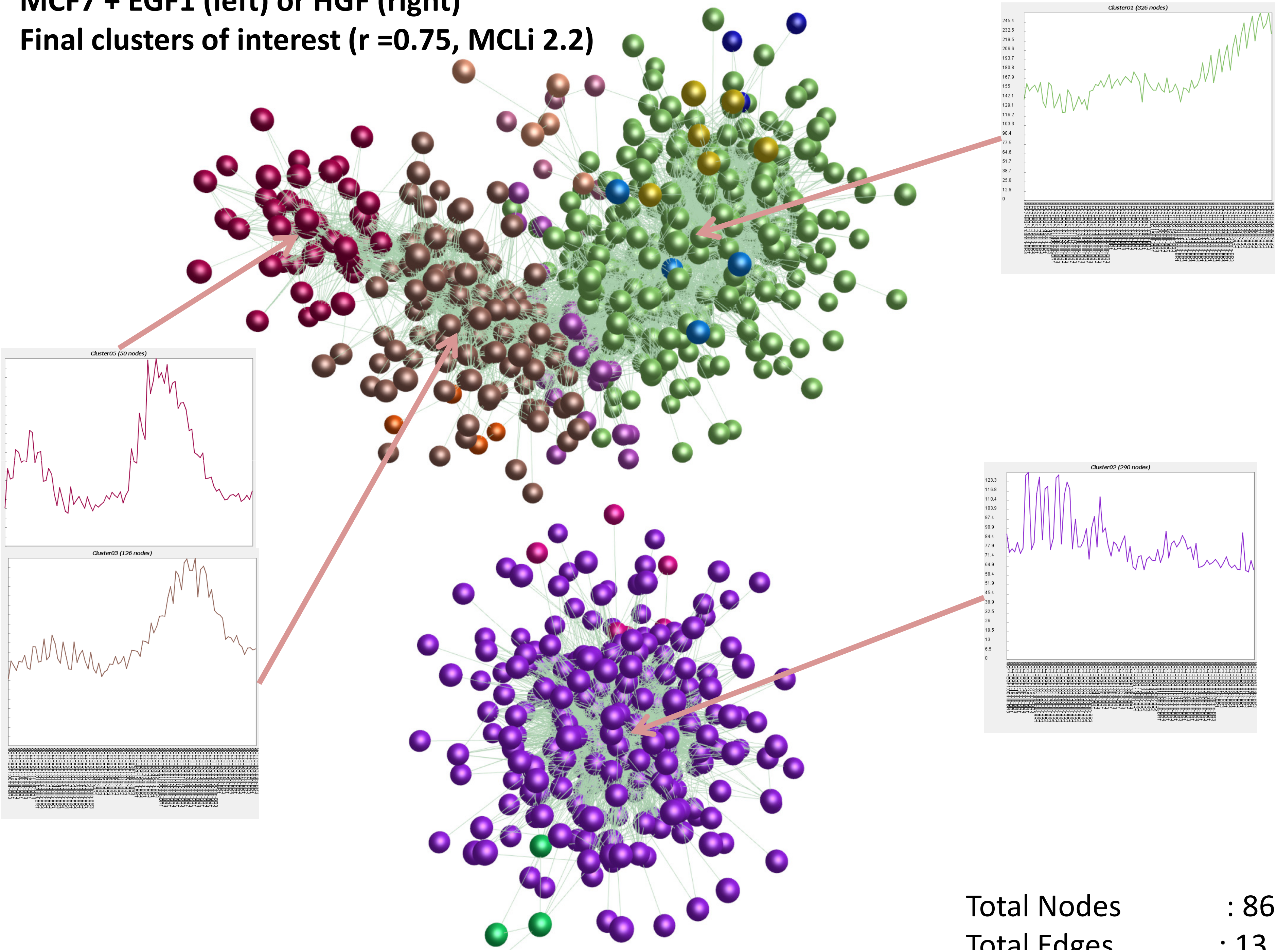
MCF7 + EGF1 or HGF
Initial graph/clusters (r =0.75, MCLi 2.2)

Many clusters due to spikes in low end data

MCF7 + EGF1 or HGF
Graph/clusters (r =0.75, MCLi 2.2),
after min 2 tags in one sample filter



MCF7 + EGF1 (left) or HGF (right)
Final clusters of interest (r =0.75, MCLi 2.2)



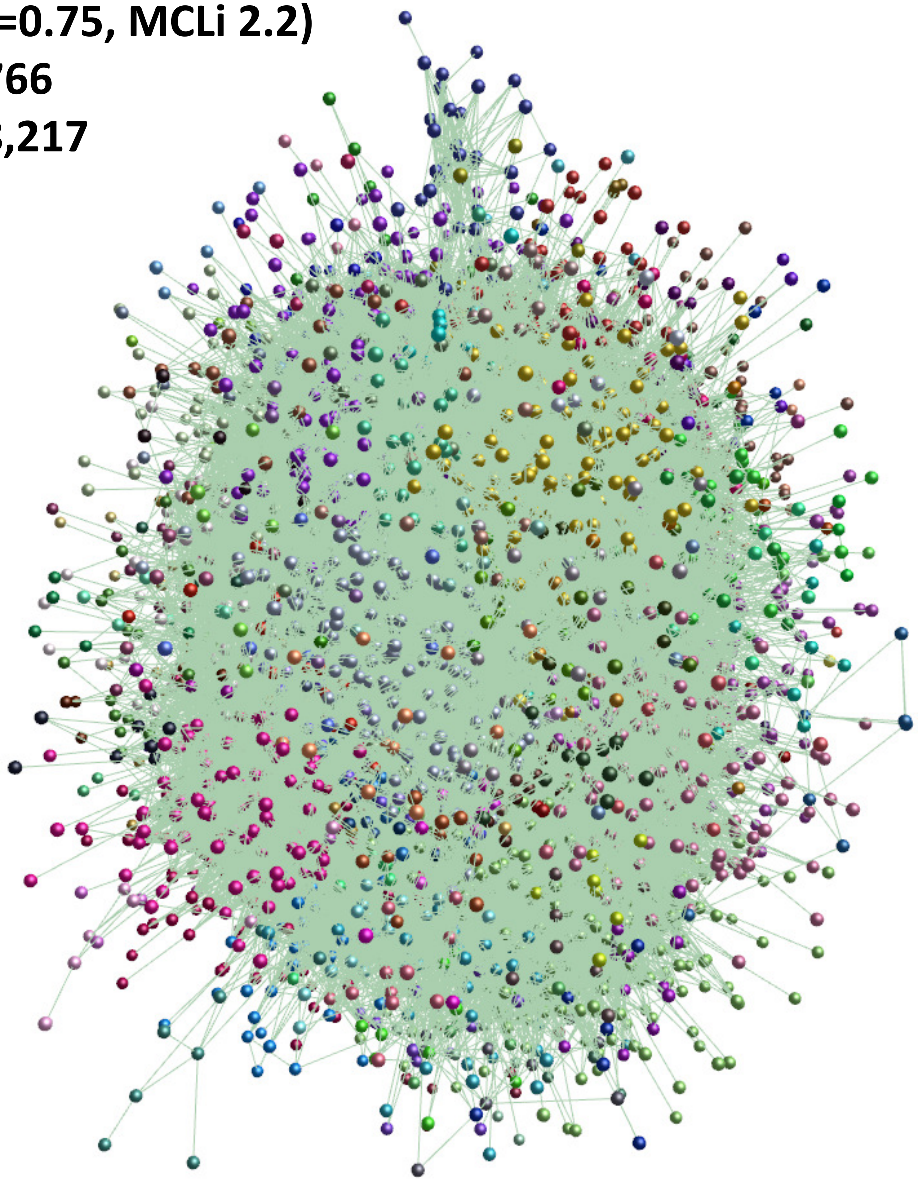
Total Nodes : 862
Total Edges : 13,75

MDM + LPS only

Initial graph/clusters (r =0.75, MCLi 2.2)

Total Nodes : 7,766

Total Edges : 348,217

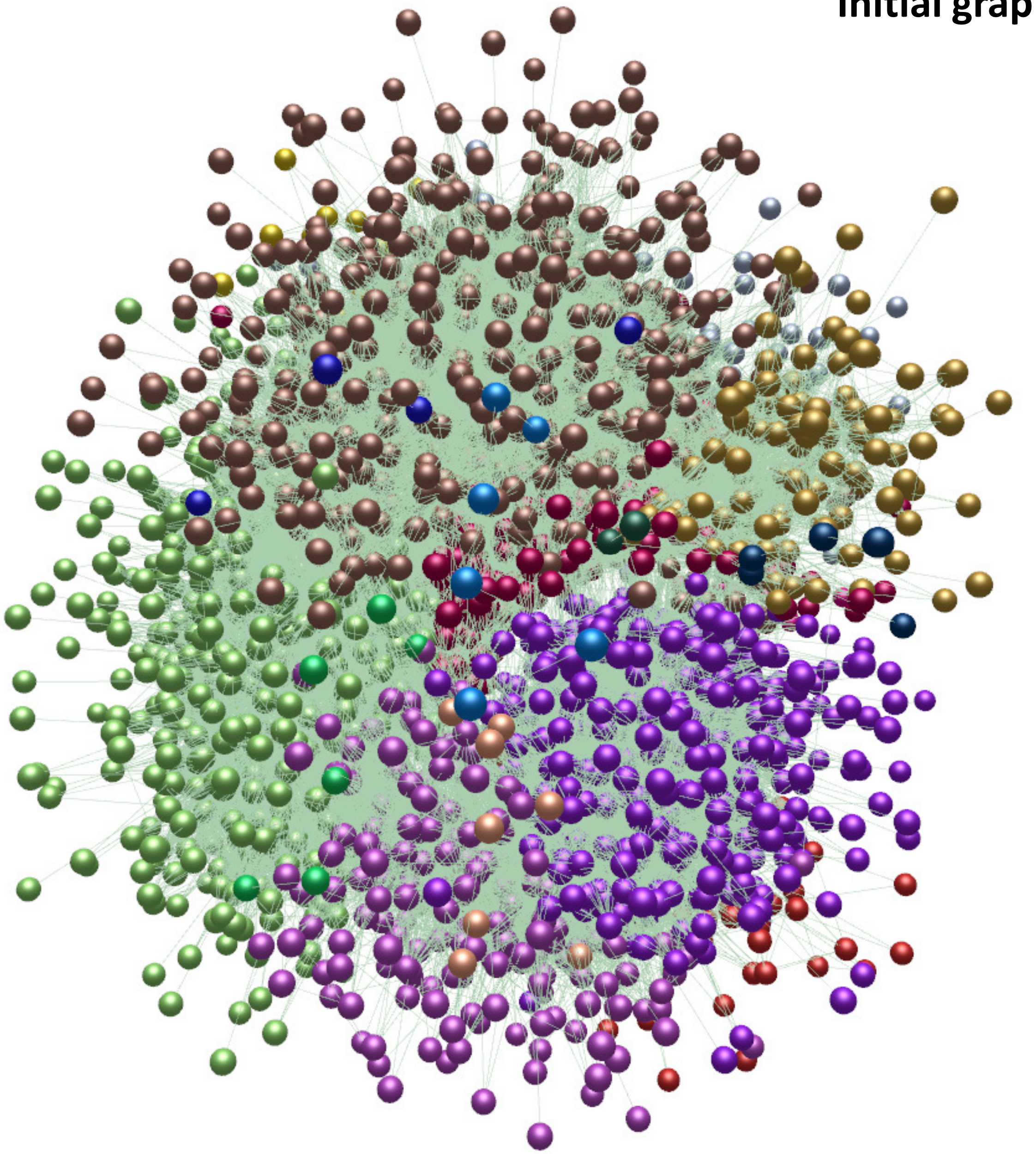


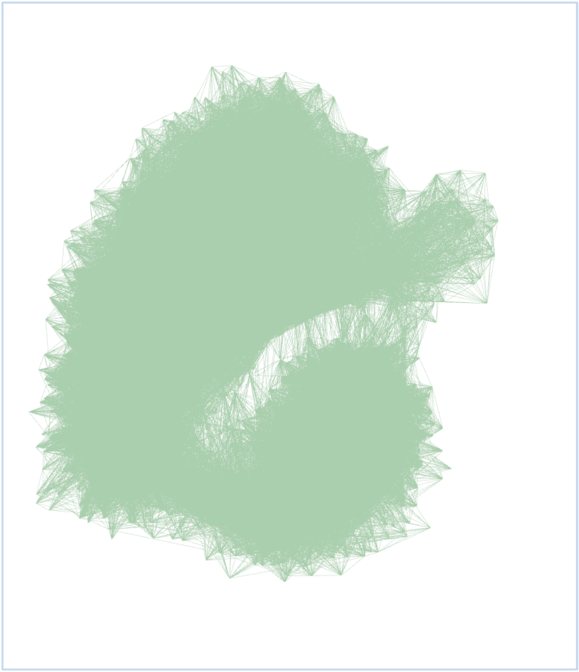
MDM + LPS only

Initial graph/clusters (r =0.75, MCLi 1.7)

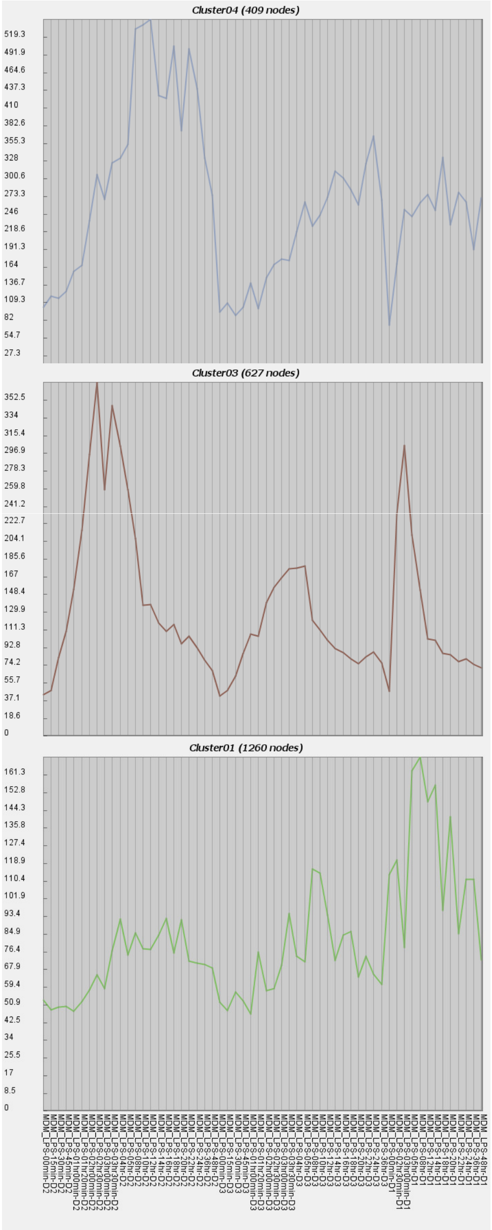
Total Nodes : 4,294

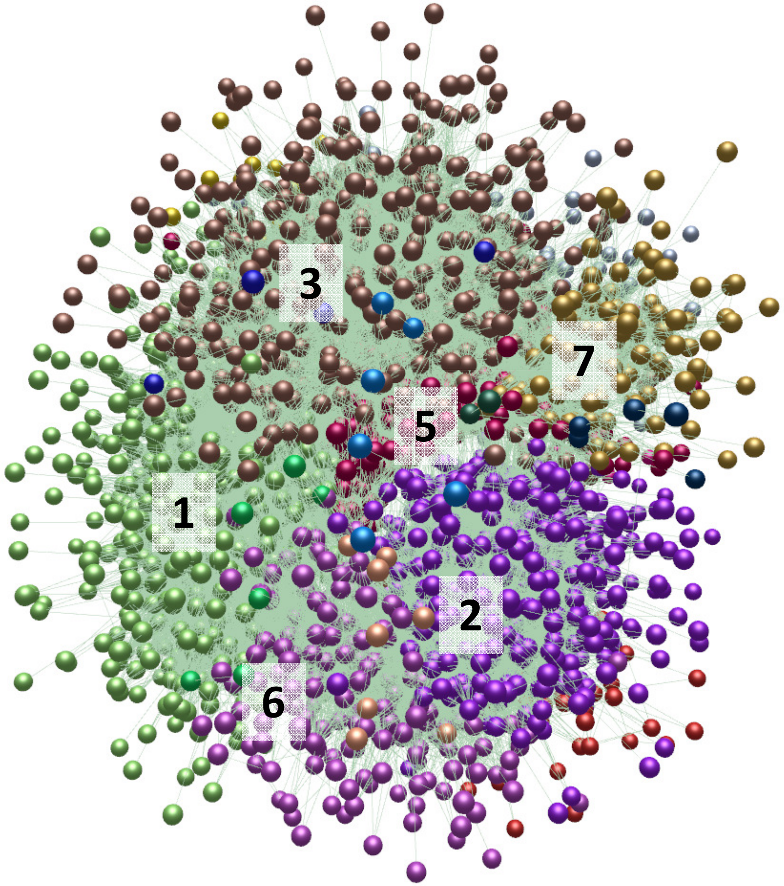
Total Edges : 204,685

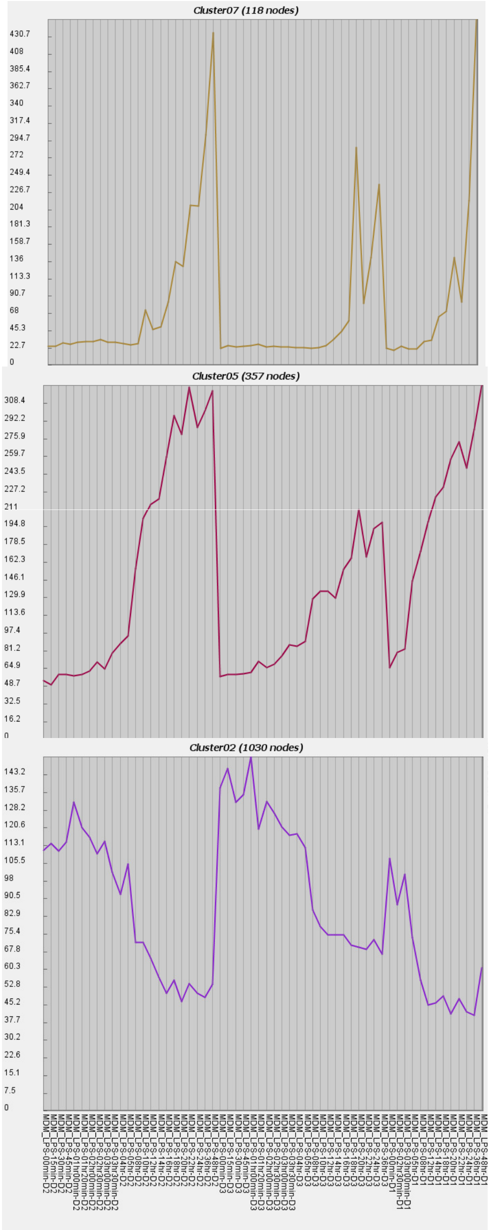




MDM + LPS only (main clusters)
Initial graph/clusters (r =0.75, MCLi 1.7)
Nodes: 4,294, Edges: 204,685



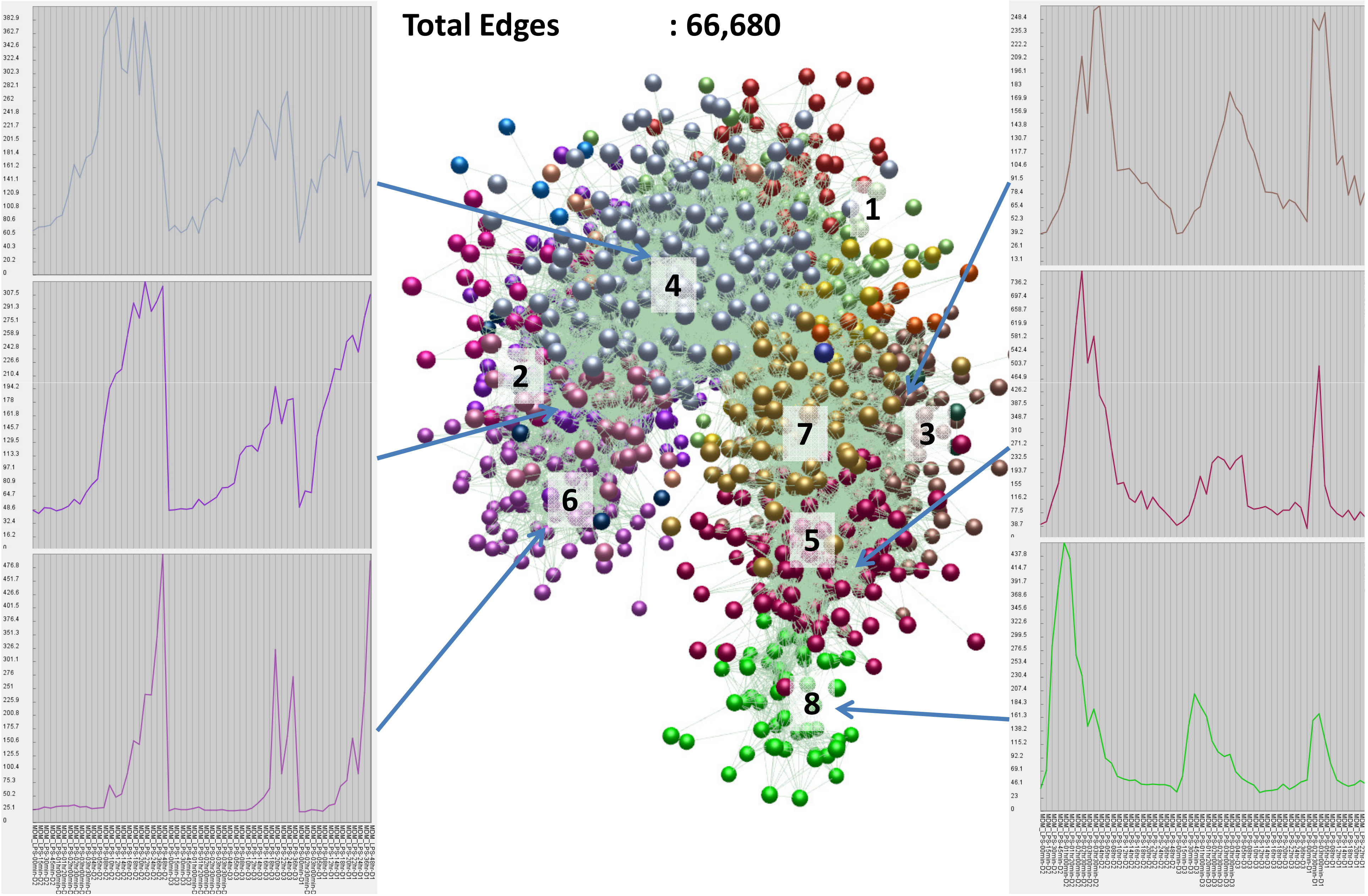




MDM + LPS GOI v2 - up regulated only
Initial graph/clusters (r =0.75, MCLi 2.2)

Total Nodes : 1,936

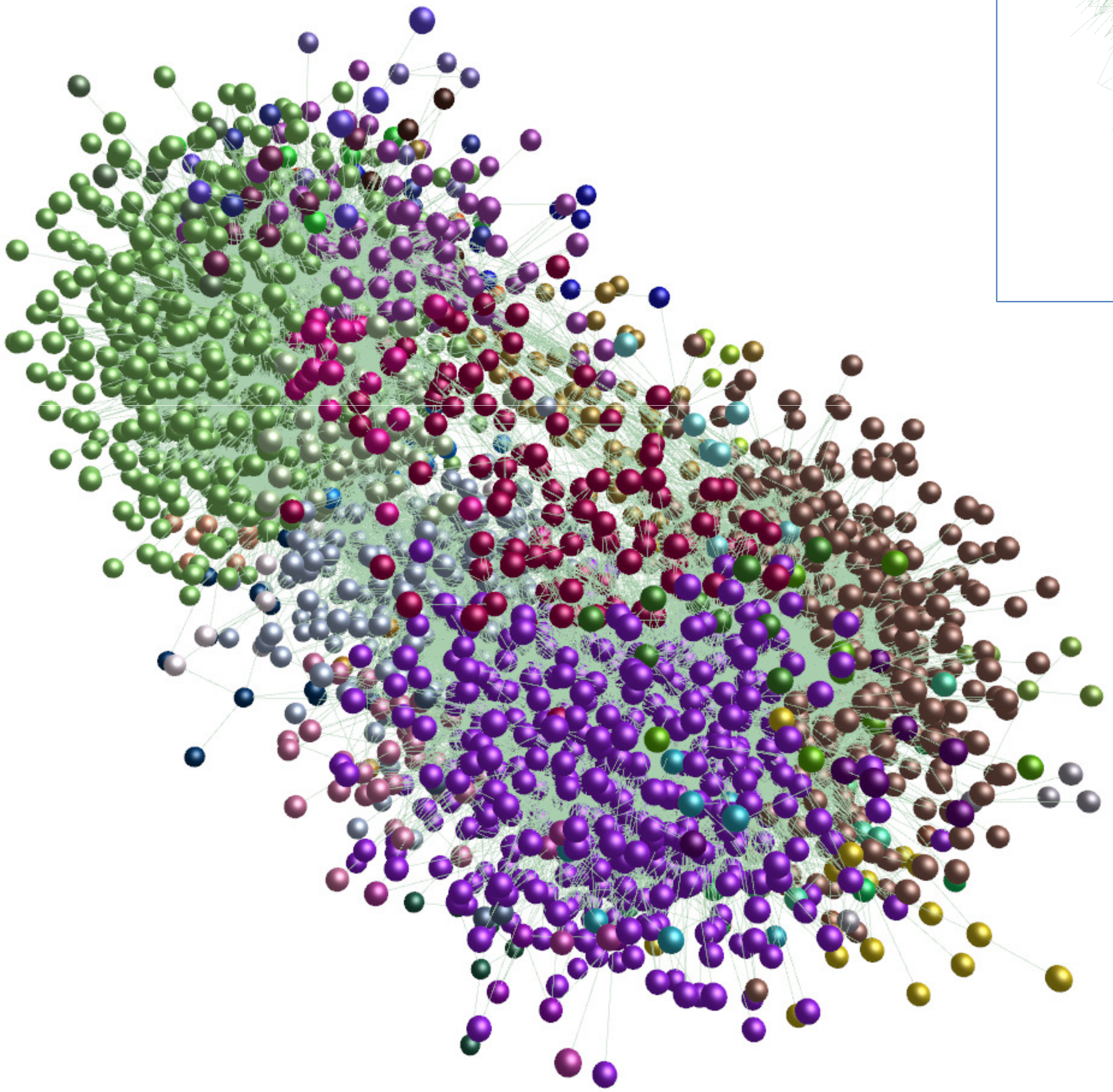
Total Edges : 66,680

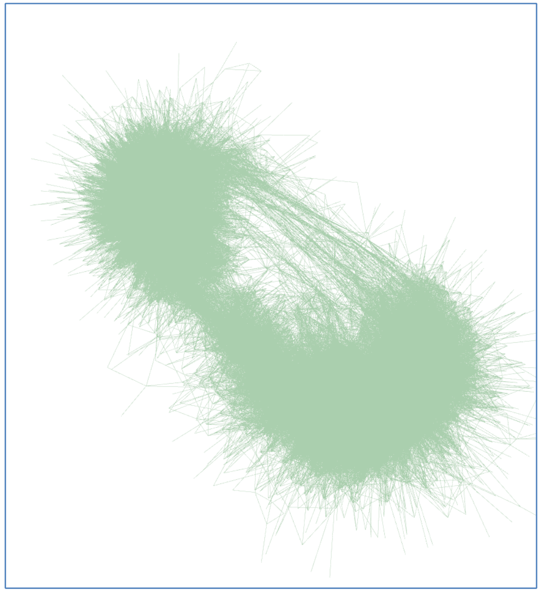


Lymph endothelial cell plus VEGF Graph/clusters (r =0.75, MCLi 1.7) after min 2 tags in one sample filter

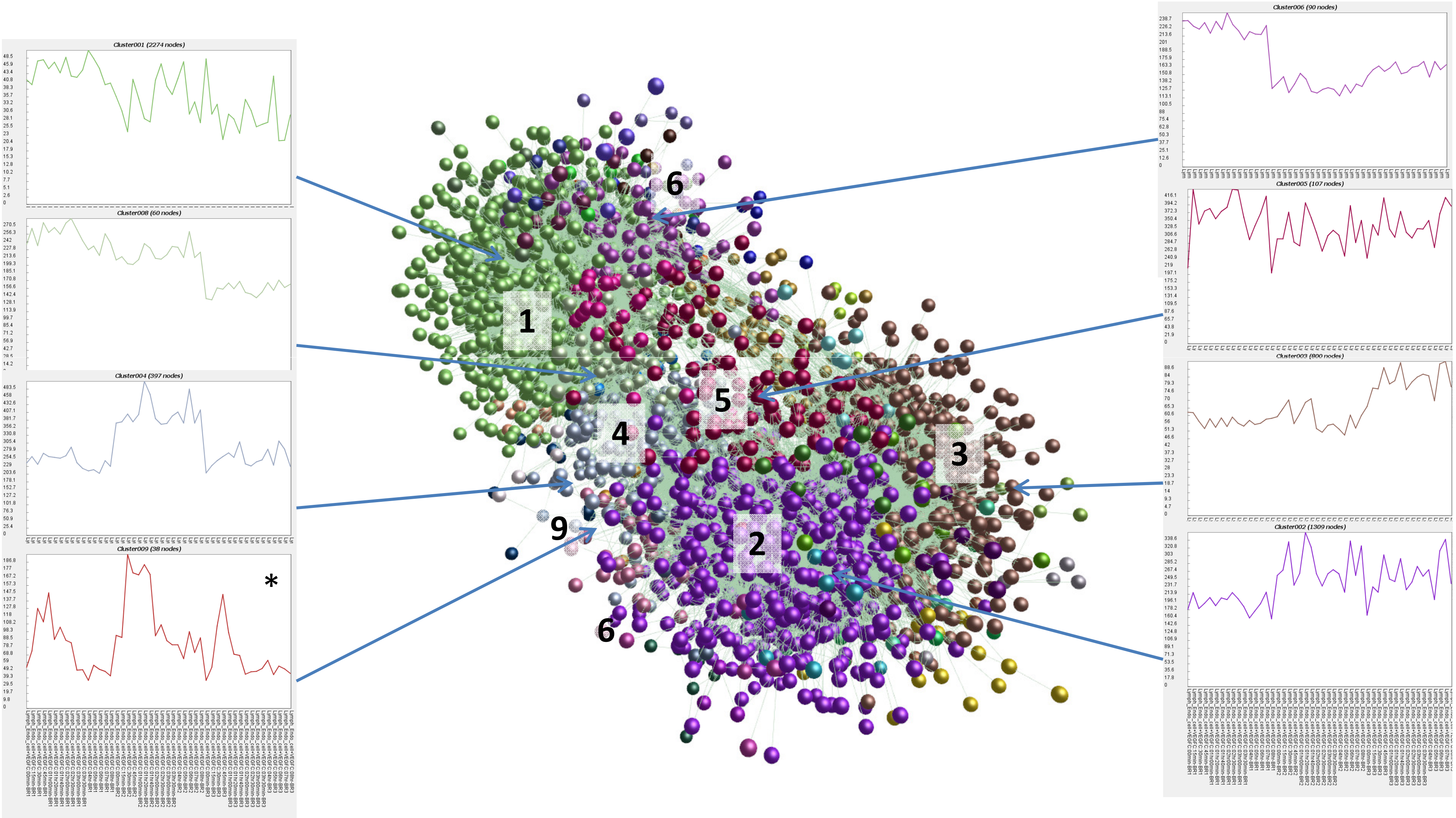
Total Nodes : 6,027

Total Edges : 612,275



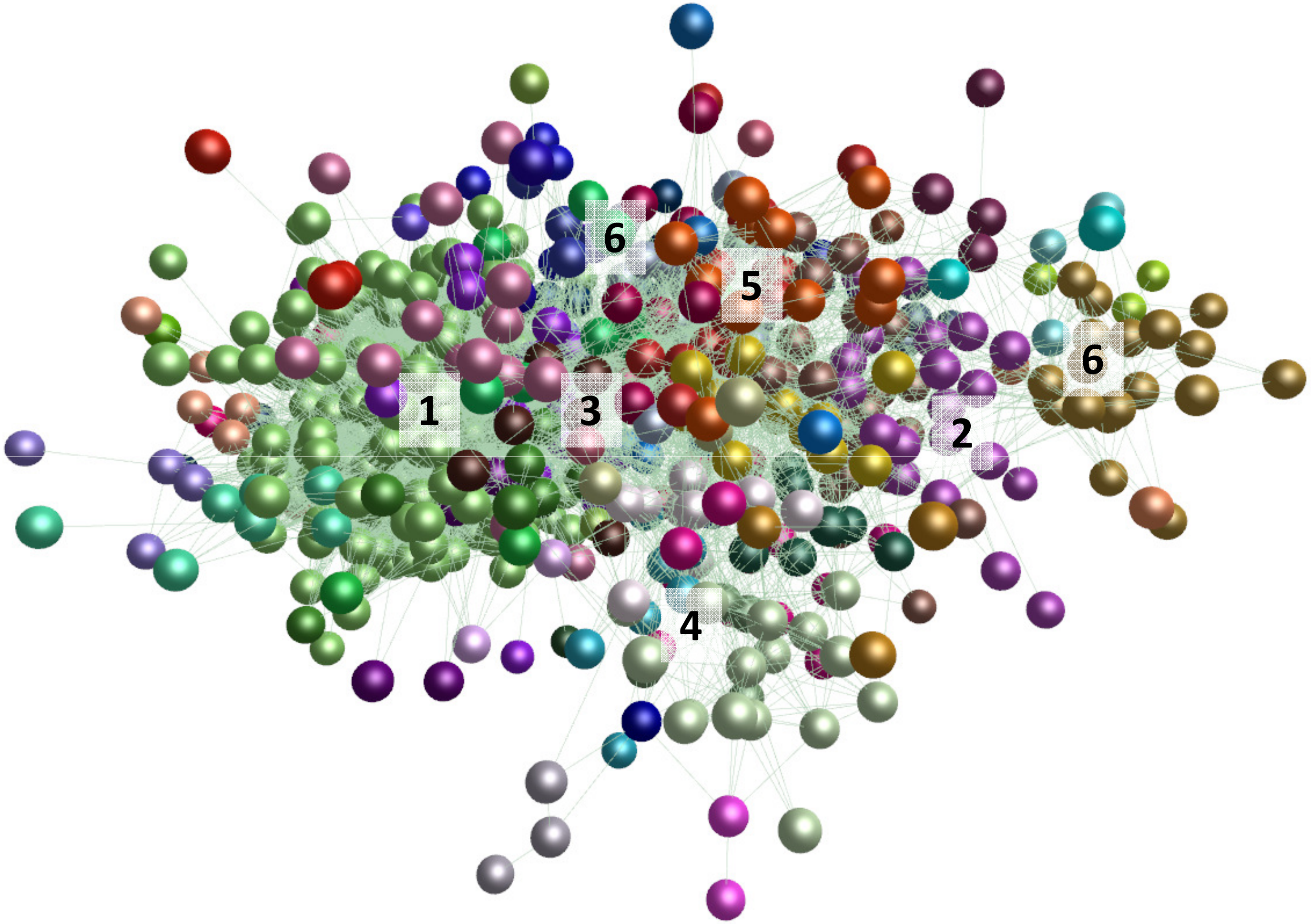


Lymph endothelial cell plus VEGF Graph/clusters (r =0.75, MCLi 1.7), after min 2 tags in one sample filter

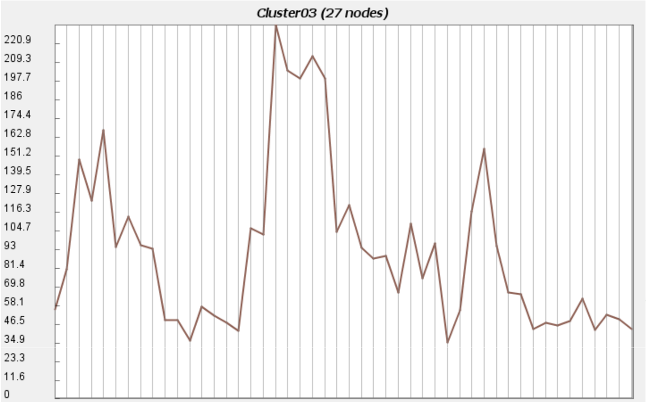


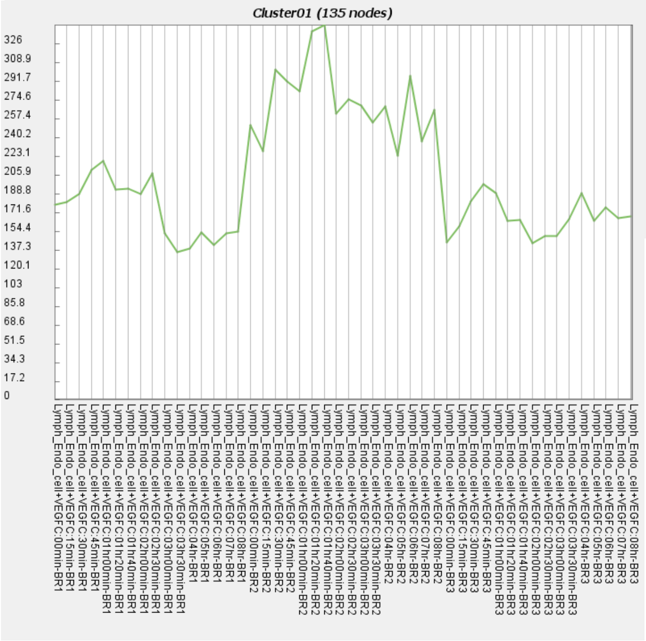
No obvious transcriptional regulation beyond 2-3 hours

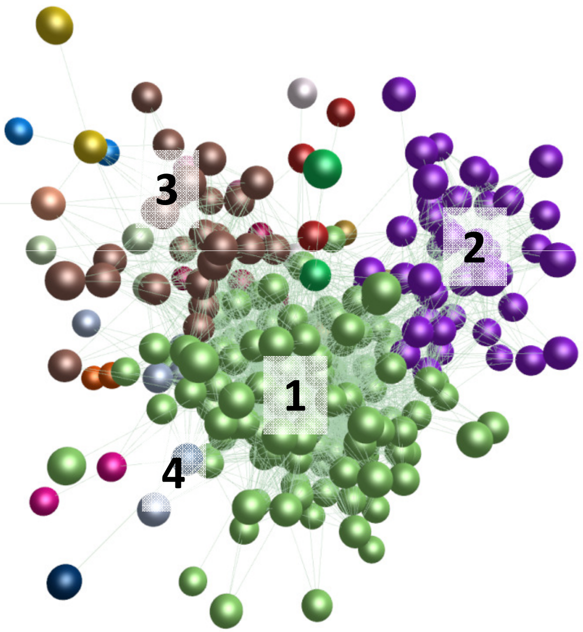
Lymph endothelial cell plus VEGF GOI v1
Based on node walk (+2) from IEGs in whole graph (cluster 9)
Graph/clusters (r =0.75, MCLi 3.0)
Data filtered to remove uninformative genes (GOI v2)

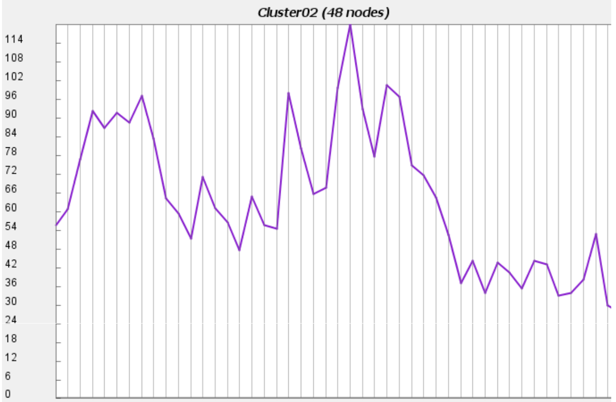


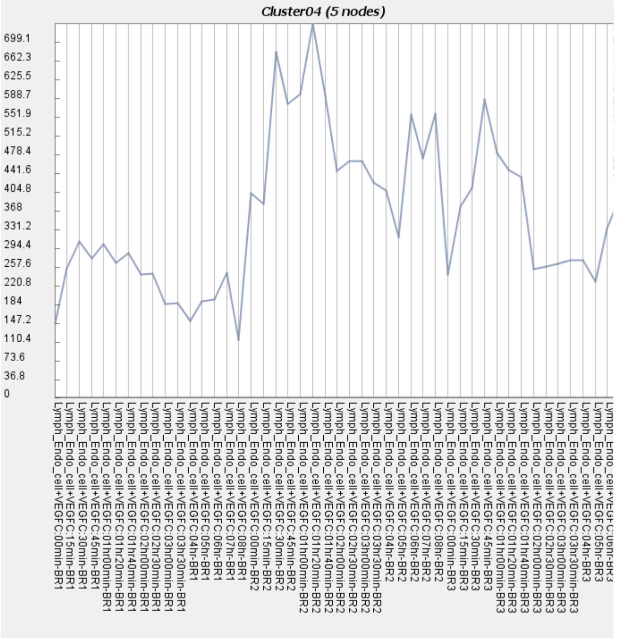
Lymph endothelial cell plus VEGF GOI v2
Graph/clusters (r =0.75, MCLi 3.0)
Nodes: 249, Edges: 4,429, 3 main clusters 15 small (<5 nodes) clusters

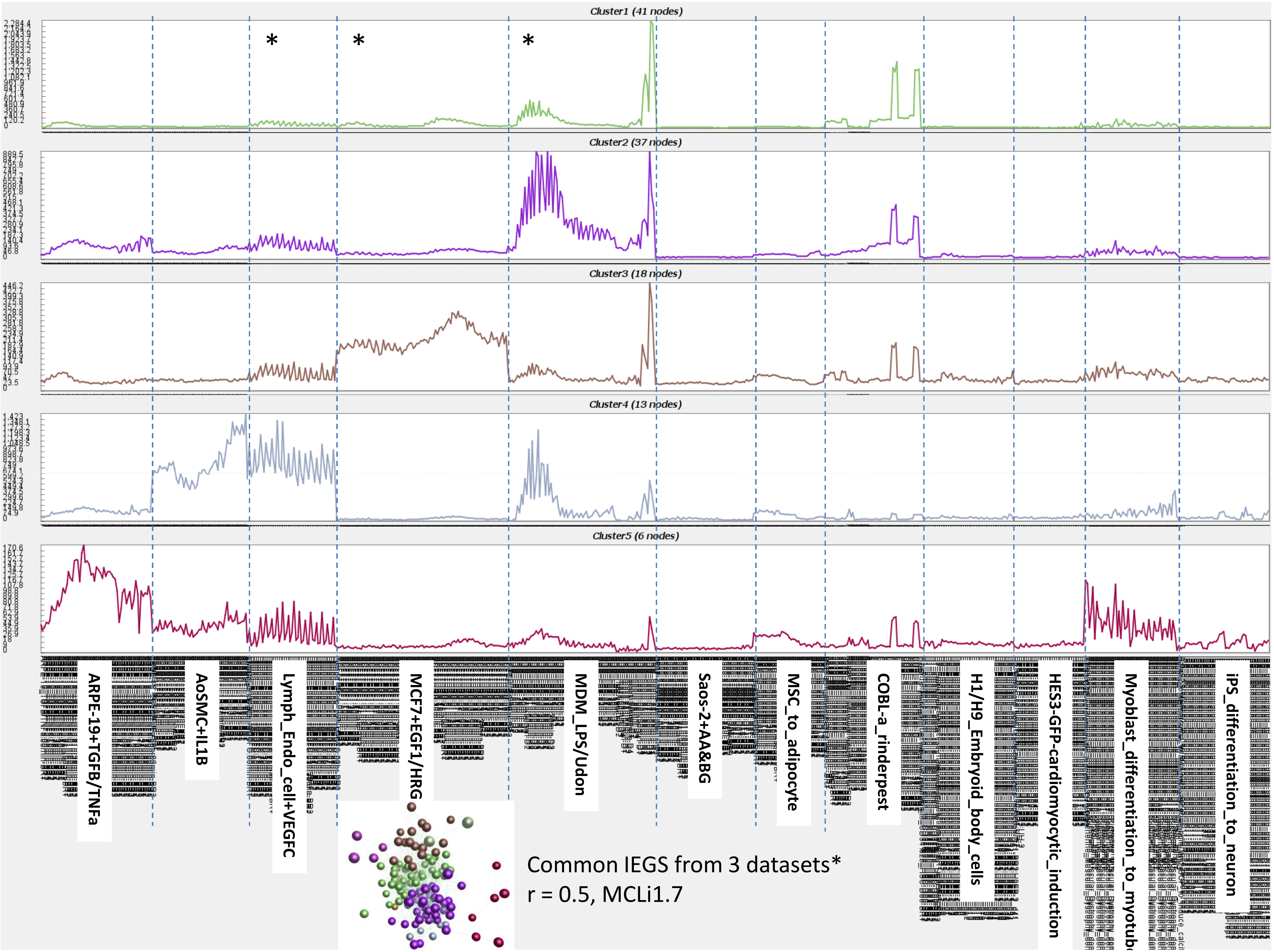












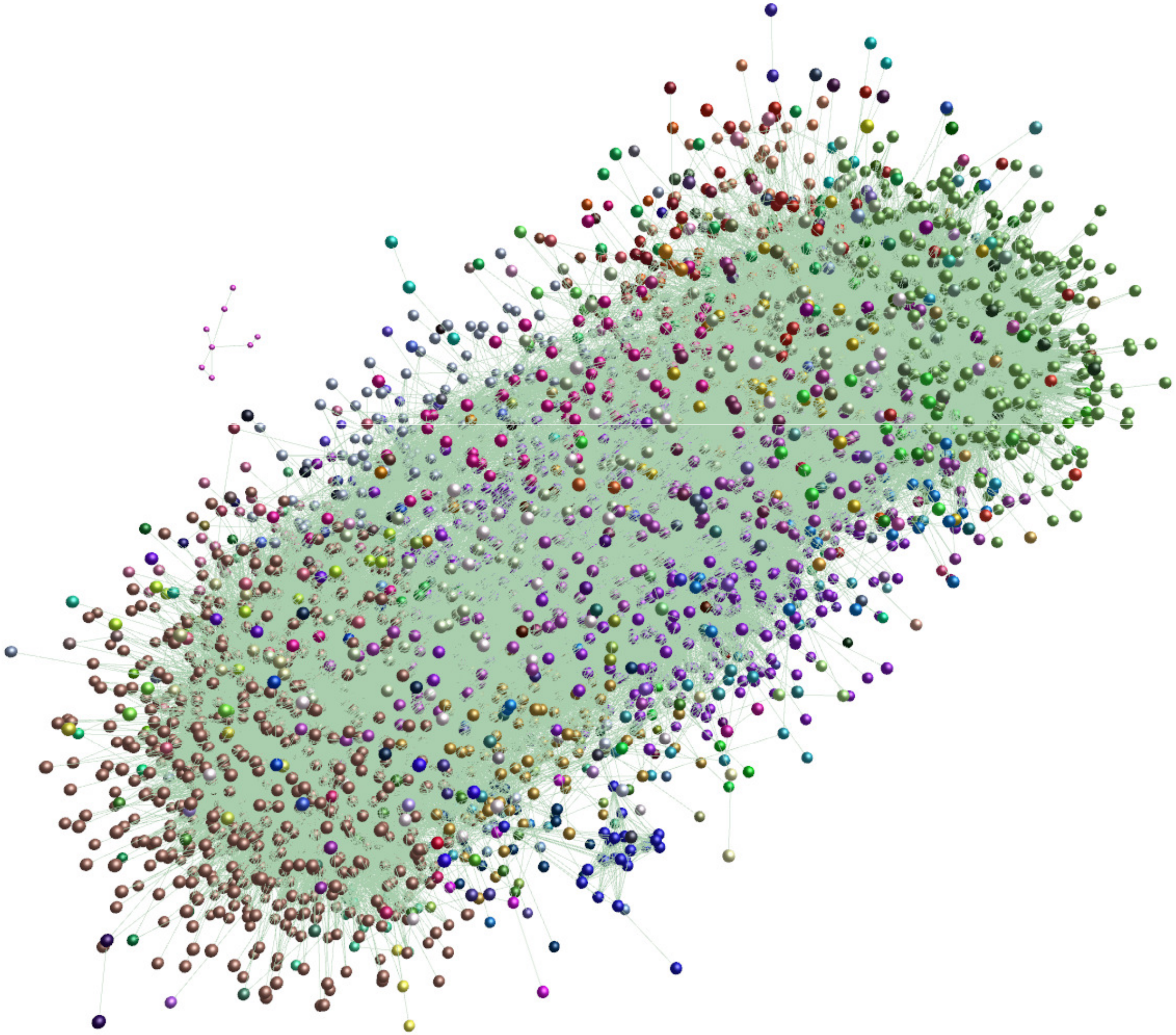
Common IEGS from 3 datasets*
r = 0.5, MCLi1.7

ARPE-19 plus TNFa

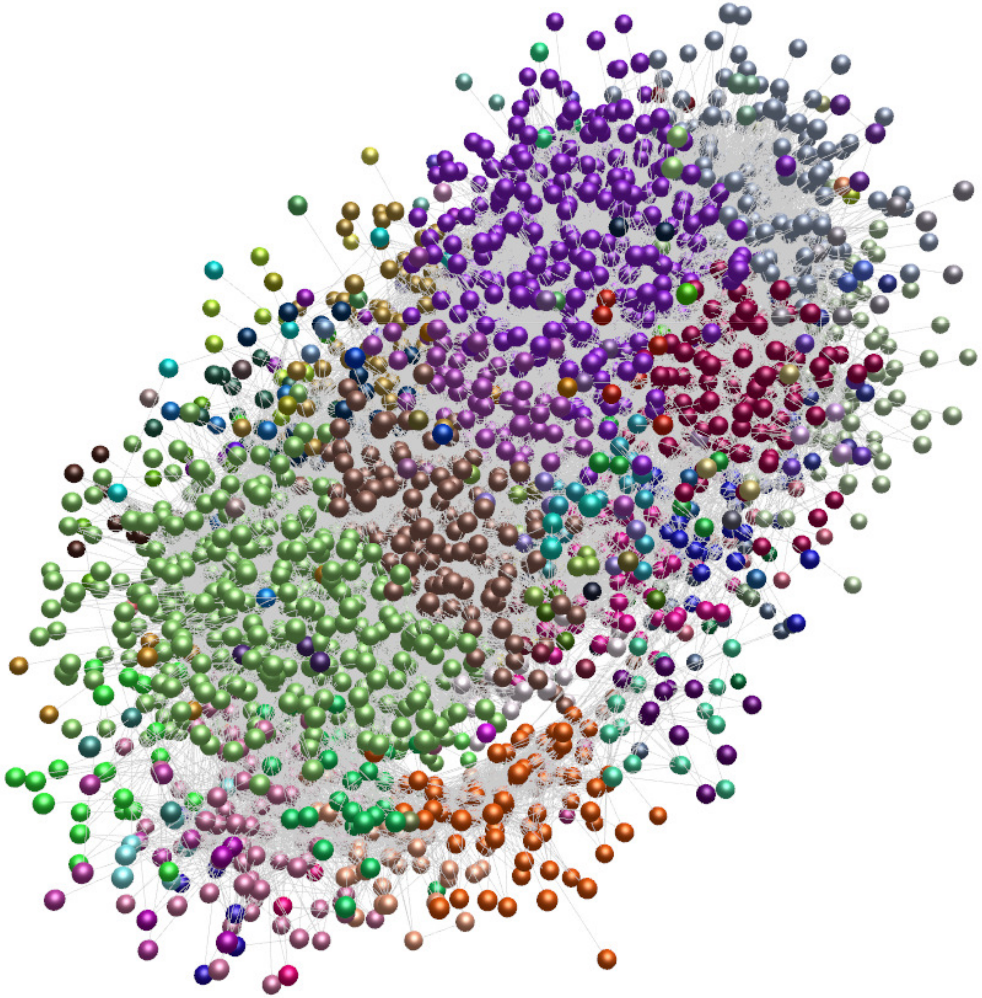
Graph/clusters (r =0.75, MCLi 1.7, filter <2 tags per gene)

Nodes: 8,929, Edges: 1,712,351

Clusters of interest selected



ARPE-19 plus TNFa GOIv1
Graph/clusters (r =0.75, MCLi 2.2)
Nodes: 5,260, Edges: 370,697
Clusters of interest selected



ARPE-19 plus TNFa GOIv2
Graph/clusters (r =0.75, MCLi 2.2, filter)
Nodes: 3,040, Edges: 277,863
Early response genes highlighted