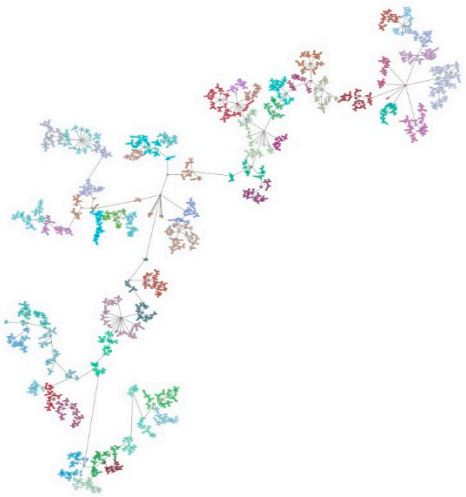
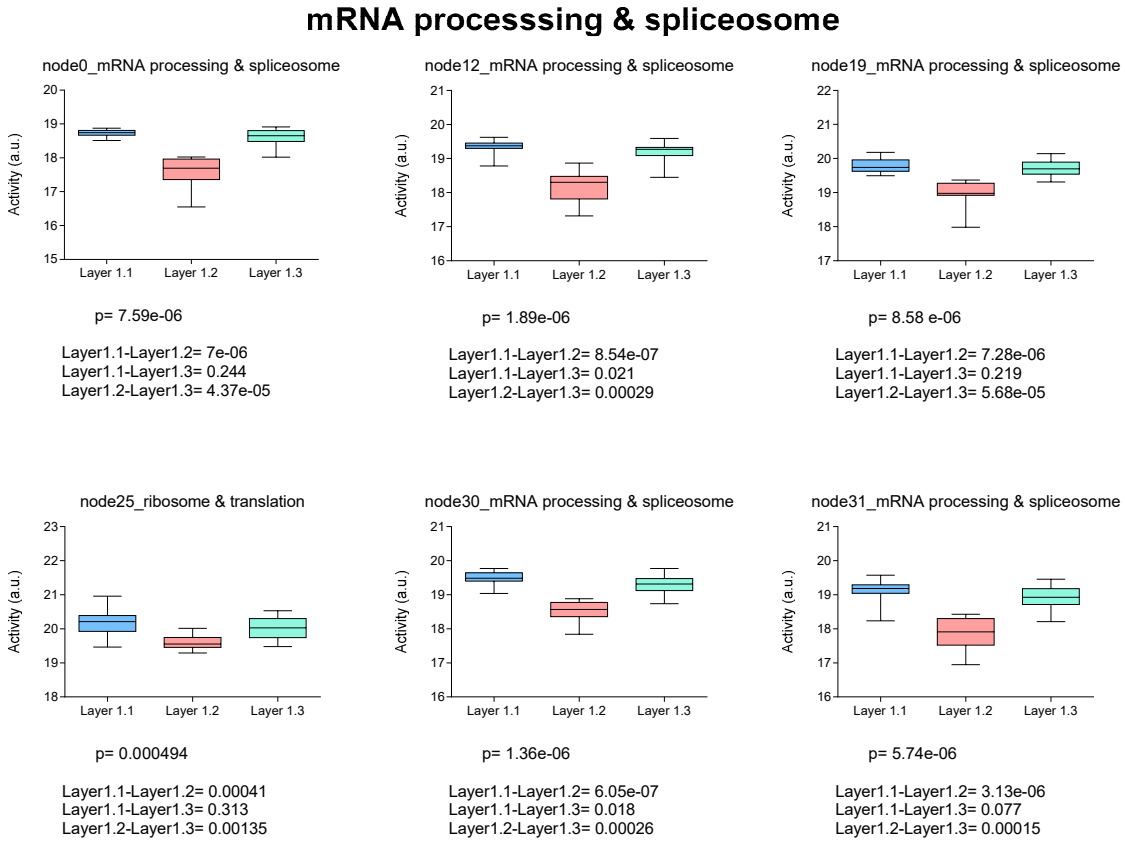
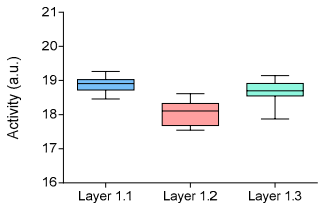


Sup Fig 1: Protein network of transurethral resection samples from EPIC muscle-invasive bladder carcinoma patients built using probabilistic graphical models. Each color represents a functional node defined by Louvain community algorithm. Functions of each node determined by gene ontology analyses can be found at Sup Table 1.



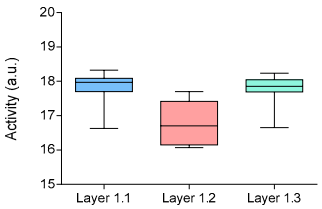
node32_mRNA processing & spliceosome



p= 1.5e-05

Layer1.1-Layer1.2= 7.88e-06
Layer1.1-Layer1.3= 0.069
Layer1.2-Layer1.3= 0.00040

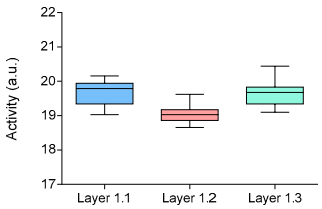
node38_RNA Processing



p= 6.96e-05

Layer1.1-Layer1.2= 8.66e-05
Layer1.1-Layer1.3= 0.436
Layer1.2-Layer1.3= 0.00014

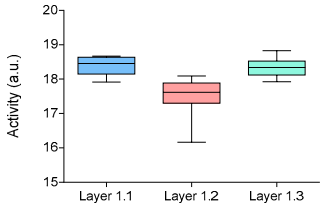
node39_mRNA transport



p= 0.00014

Layer1.1-Layer1.2= 0.00015
Layer1.1-Layer1.3= 0.393
Layer1.2-Layer1.3= 0.00033

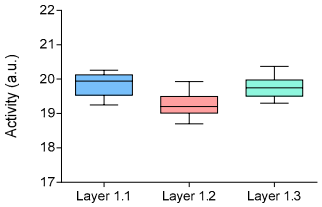
node42_RNA transport



p= 2.61e-05

Layer1.1-Layer1.2= 3.37e-05
Layer1.1-Layer1.3= 0.413
Layer1.2-Layer1.3= 6.35e-05

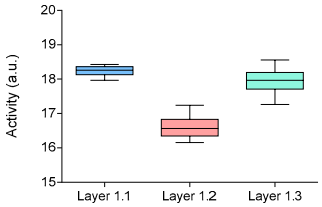
node45_mRNA processing & spliceosome



p= 0.00092

Layer1.1-Layer1.2= 0.00071
Layer1.1-Layer1.3= 0.278
Layer1.2-Layer1.3= 0.00278

node47_endoplasmic reticulum transport

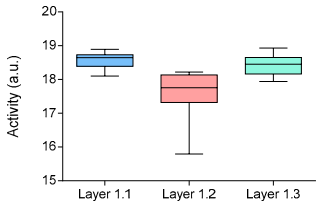


p= 1.03e-07

Layer1.1-Layer1.2= 5.07e-08
Layer1.1-Layer1.3= 0.0017
Layer1.2-Layer1.3= 0.00041

Proliferation

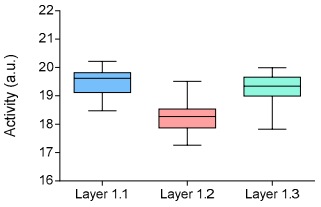
node1_regulation of nucleotide-excision repair, regulation of cell cycle



p= 2.42e-05

Layer1.1-Layer1.2= 1.26e-05
Layer1.1-Layer1.3= 0.063
Layer1.2-Layer1.3= 0.00067

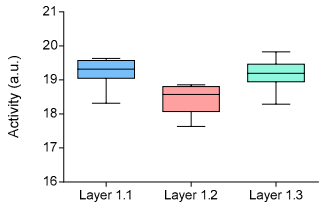
node13_cell-cell adhesion, cell migration



p= 0.00014

Layer1.1-Layer1.2= 0.0001
Layer1.1-Layer1.3= 0.203
Layer1.2-Layer1.3= 0.00078

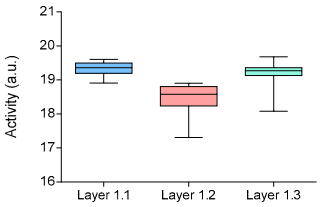
node17_DNA repair



p= 0.000123

Layer1.1-Layer1.2= 0.000132
Layer1.1-Layer1.3= 0.39
Layer1.2-Layer1.3= 0.00028

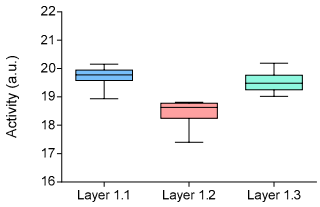
node18_DNA replication



p= 1.21e-05

Layer1.1-Layer1.2= 7.88e-06
Layer1.1-Layer1.3= 0.137
Layer1.2-Layer1.3= 0.000143

node52_telomeres, microtubules

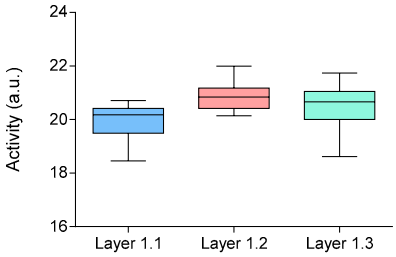


p= 1.37e-06

Layer1.1-Layer1.2= 6.32e-07
Layer1.1-Layer1.3= 0.032
Layer1.2-Layer1.3= 0.00013

Immune response

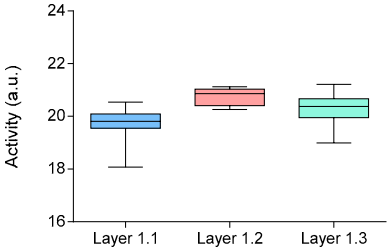
node4_adaptive immune response, antigen binding, immunoglobulin



p= 0.0029

Layer1.1-Layer1.2= 0.0073
Layer1.1-Layer1.3= 0.0077
Layer1.2-Layer1.3= 0.281

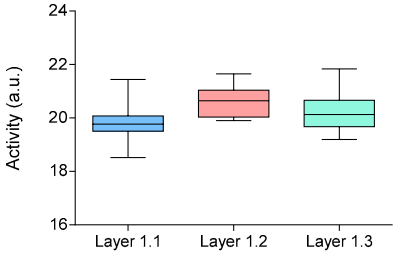
node5_Immune response, defense response



p= 8.67e-05

Layer1.1-Layer1.2= 9.29e-05
Layer1.1-Layer1.3= 0.0048
Layer1.2-Layer1.3= 0.028

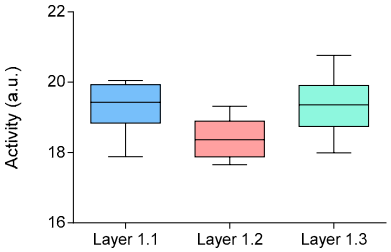
node6_Immune response



p= 0.025

Layer1.1-Layer1.2= 0.024
Layer1.1-Layer1.3= 0.127
Layer1.2-Layer1.3= 0.131

node7_Immune response, defense response

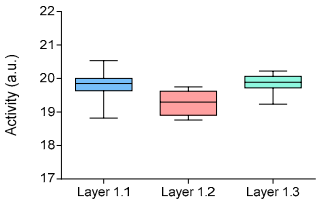


p= 0.0065

Layer1.1-Layer1.2= 0.005
Layer1.1-Layer1.3= 0.863
Layer1.2-Layer1.3= 0.005

Metabolism

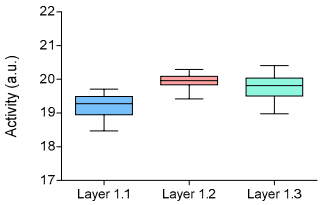
node14_metabolic process



p= 0.00081

Layer1.1-Layer1.2= 0.0045
Layer1.1-Layer1.3= 0.479
Layer1.2-Layer1.3= 0.00052

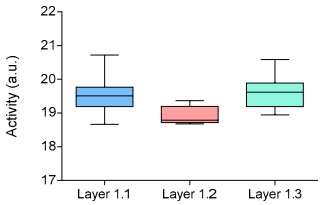
node16_cellular detoxification



p= 7.56e-06

Layer1.1-Layer1.2= 5.35e-05
Layer1.1-Layer1.3= 5.35e-05
Layer1.2-Layer1.3= 0.23

node46_mitochondrial metabolism

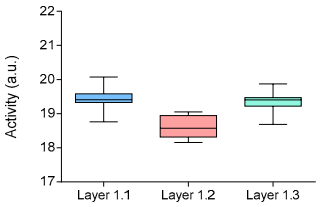


p= 0.00046

Layer1.1-Layer1.2= 0.00442
Layer1.1-Layer1.3= 0.369
Layer1.2-Layer1.3= 0.000278

Ribosome &translation

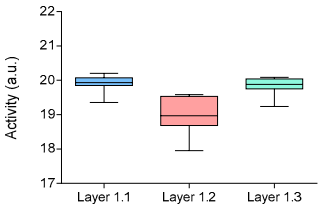
node21_ribosome & translation



p= 2.76 e-05

Layer1.1-Layer1.2= 3.91e-05
Layer1.1-Layer1.3= 0.454
Layer1.2-Layer1.3= 5.28e-05

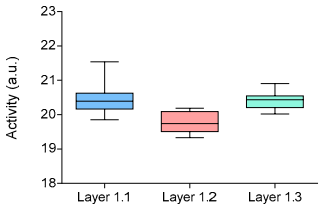
node22_ribosome & translation



p= 2.76 e-05

Layer1.1-Layer1.2= 2.7e-05
Layer1.1-Layer1.3= 0.314
Layer1.2-Layer1.3= 9.54e-05

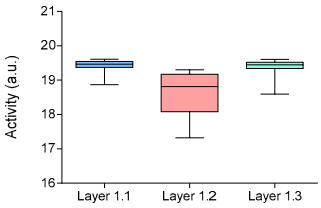
node23_ribosome & translation



p= 0.000148

Layer1.1-Layer1.2= 0.00034
Layer1.1-Layer1.3= 0.919
Layer1.2-Layer1.3= 0.000153

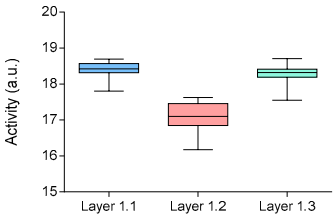
node24_ribosome & translation



p= 0.000102

Layer1.1-Layer1.2= 0.00012
Layer1.1-Layer1.3= 0.452
Layer1.2-Layer1.3= 0.000196

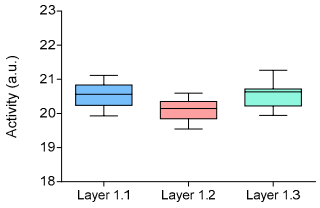
node28_rRNA Processing, nucleic acid catabolic process



p= 2.77e-06

Layer1.1-Layer1.2= 1.42e-06
Layer1.1-Layer1.3= 0.058
Layer1.2-Layer1.3= 0.00017

node29_ribosome & translation

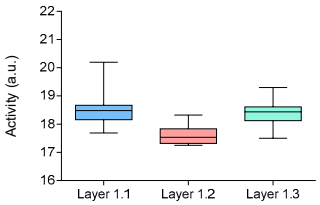


p= 0.0098

Layer1.1-Layer1.2= 0.0094
Layer1.1-Layer1.3= 0.944
Layer1.2-Layer1.3= 0.0094

Others

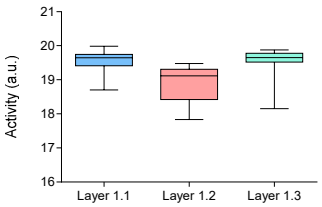
node33_mitochondrial translation



p= 0.00013

Layer1.1-Layer1.2= 0.00022
Layer1.1-Layer1.3= 0.933
Layer1.2-Layer1.3= 0.00017

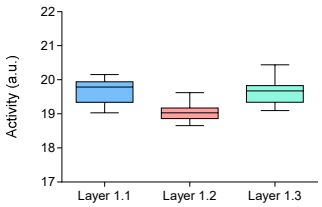
node36_GTPase activity, endosome



p= 0.00038

Layer1.1-Layer1.2= 0.00095
Layer1.1-Layer1.3= 0.823
Layer1.2-Layer1.3= 0.00034

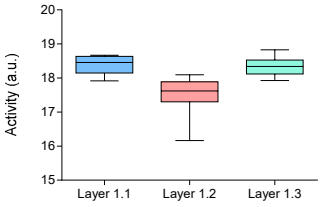
node39_mRNA transport



p= 0.00014

Layer1.1-Layer1.2= 0.00015
Layer1.1-Layer1.3= 0.393
Layer1.2-Layer1.3= 0.00033

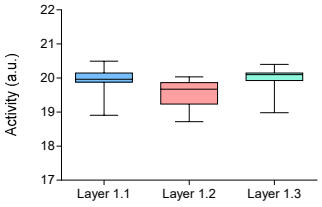
node42_RNA transport



p= 2.61e-05

Layer1.1-Layer1.2= 3.37e-05
Layer1.1-Layer1.3= 0.413
Layer1.2-Layer1.3= 6.35e-05

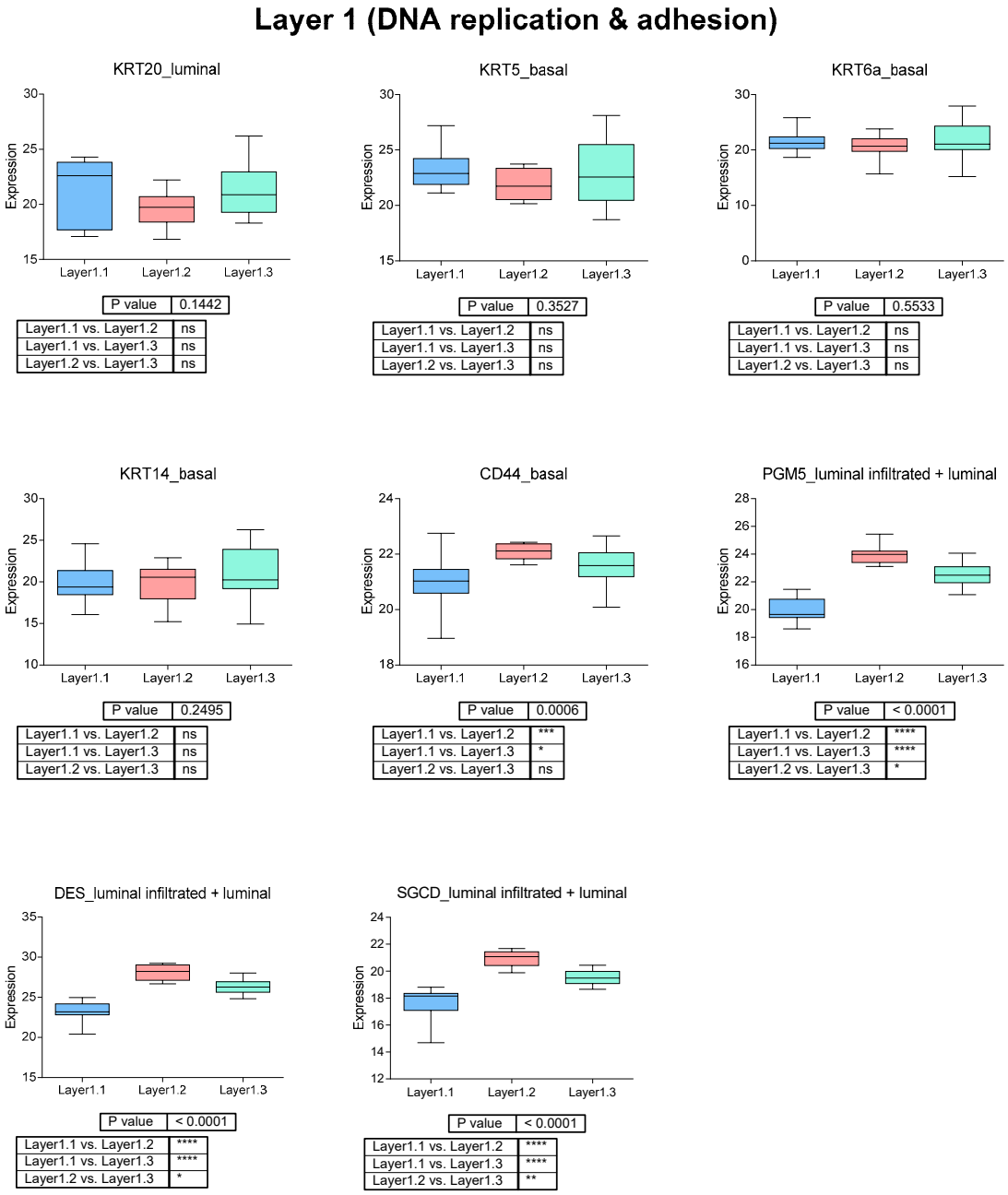
node47_endoplasmic reticulum transport



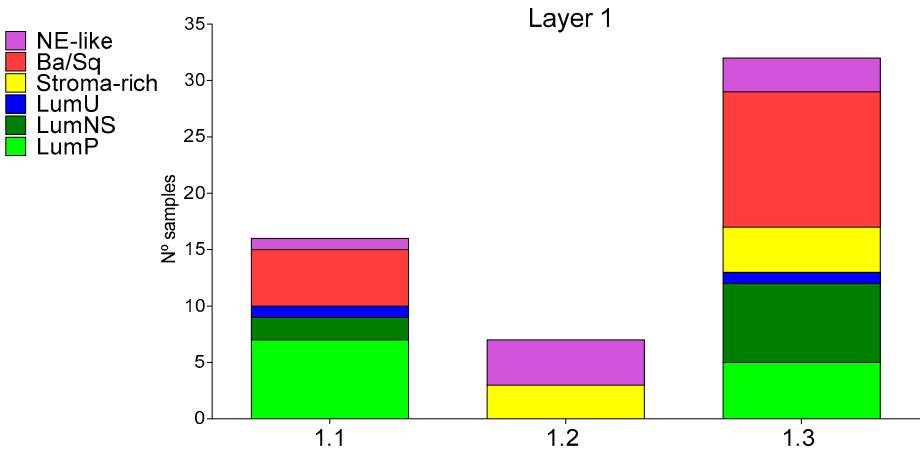
p= 0.0018

Layer1.1-Layer1.2= 0.00115
Layer1.1-Layer1.3= 0.39
Layer1.2-Layer1.3= 0.00116

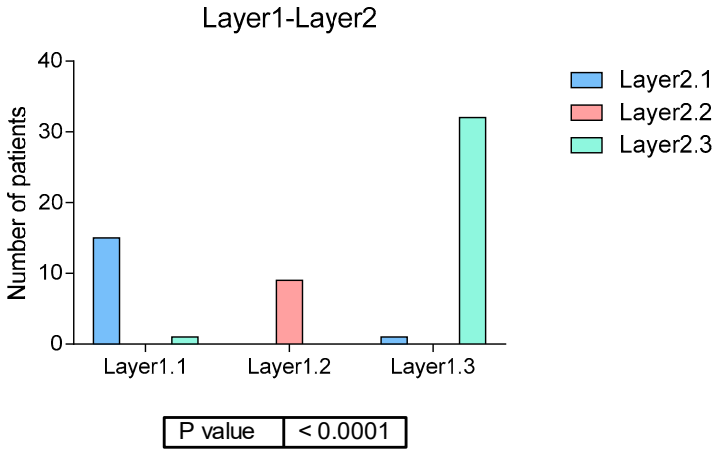
Sup Fig 2: Differential functional node activities in EPIC-MIBC TURBT samples according to Layer1 groups.



Sup Fig 3: Expression of luminal and basal biomarkers in Layer1 groups in EPIC-MIBC TURBT samples. ns $p > 0.05$; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$; **** $p \leq 0.0001$.

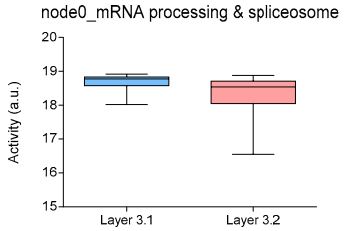


Sup Fig 4: Distribution of MIBC consensus molecular subtypes in Layer1 groups of EPIC-MIBC TURBT samples.

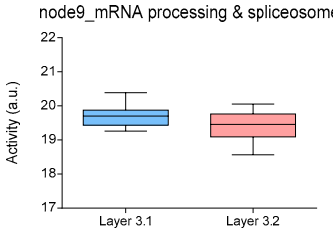


Sup Fig 5: Distribution of Layer1 and Layer2 classifications.

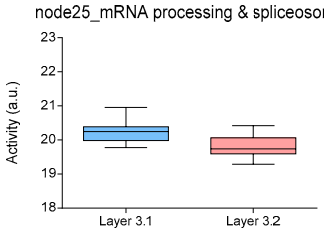
mRNA processing



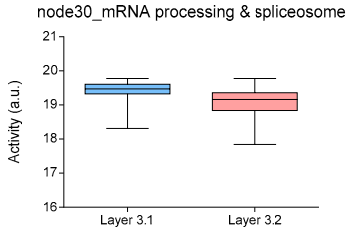
p=0.0013



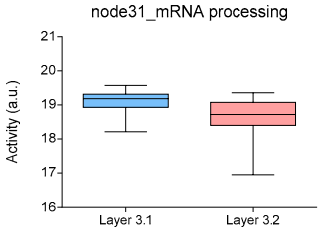
p=0.015



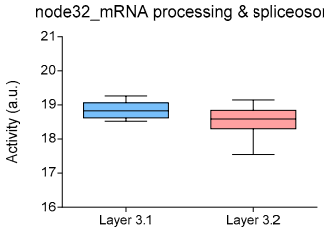
p=0.0



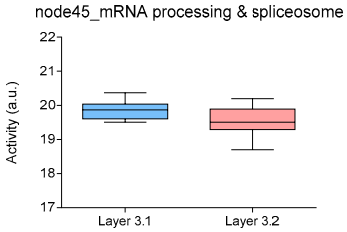
p=0.0015



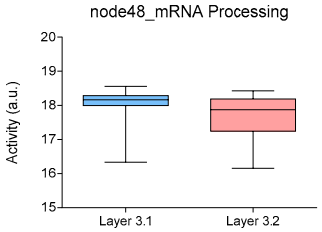
p=0.00019



p=0.0016

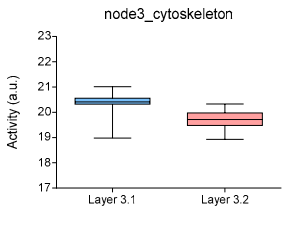


p=0.0033

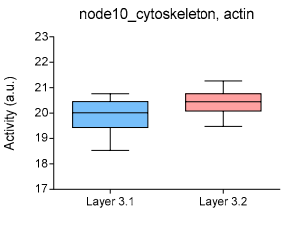


p=0.0169

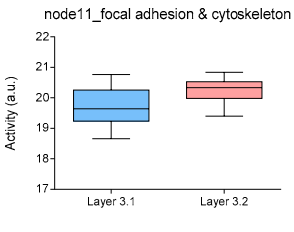
Cytoskeleton



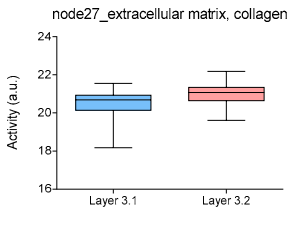
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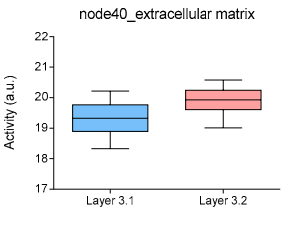
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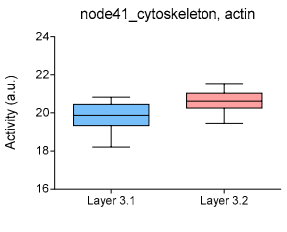
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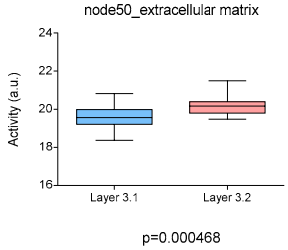
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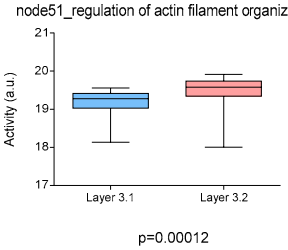
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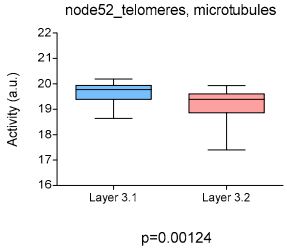
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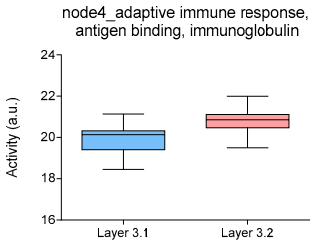


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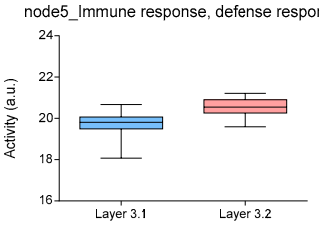


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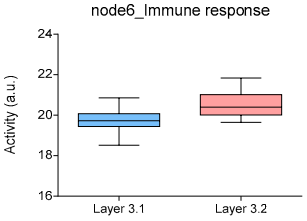
Immune response



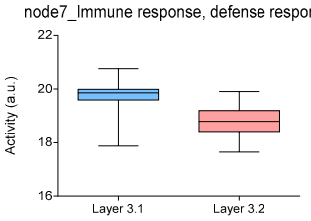
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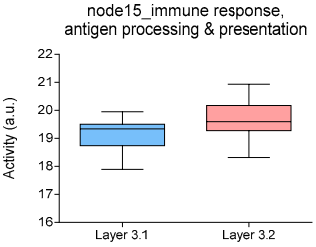
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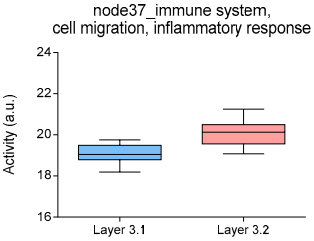
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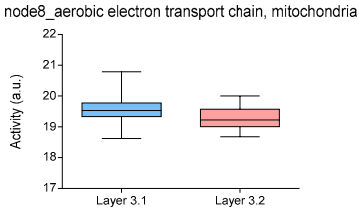


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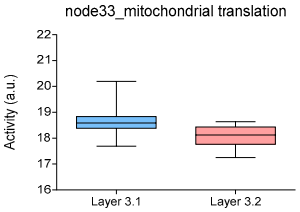


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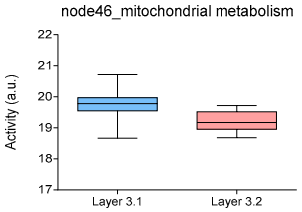
Mitochondria



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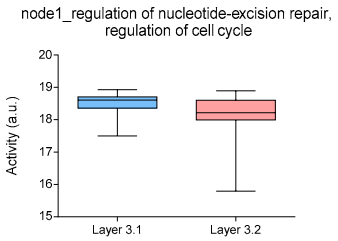


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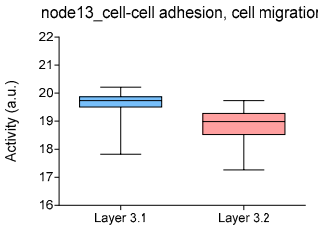


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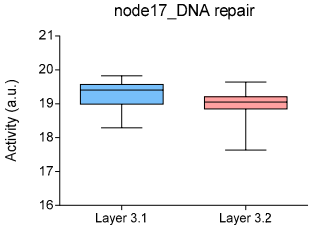
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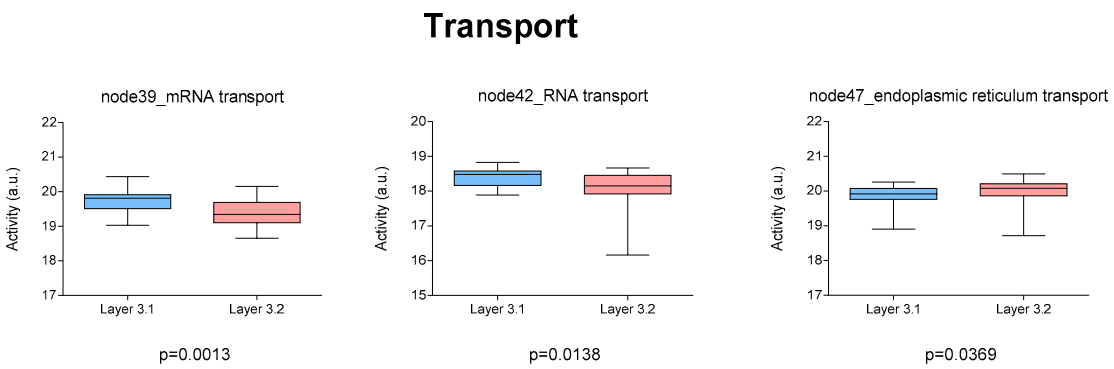
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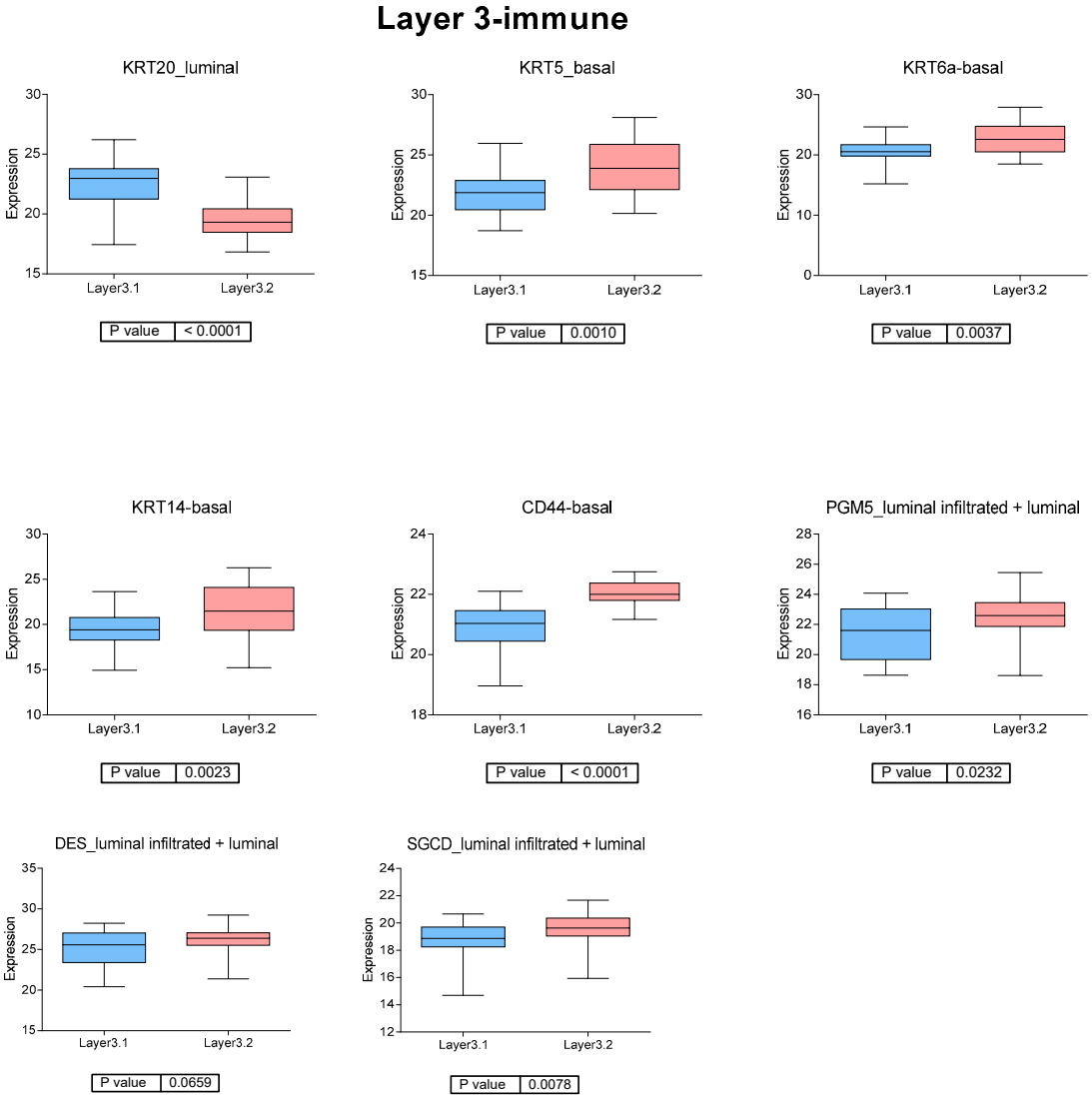
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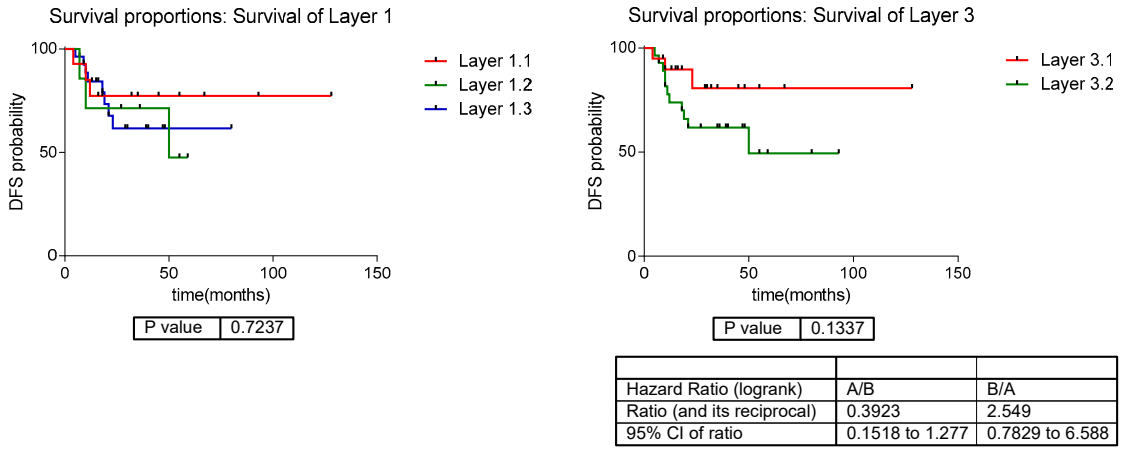
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Sup Fig 6: Differential functional node activities in EPIC-MIBC TURBT samples according to Layer3 groups.

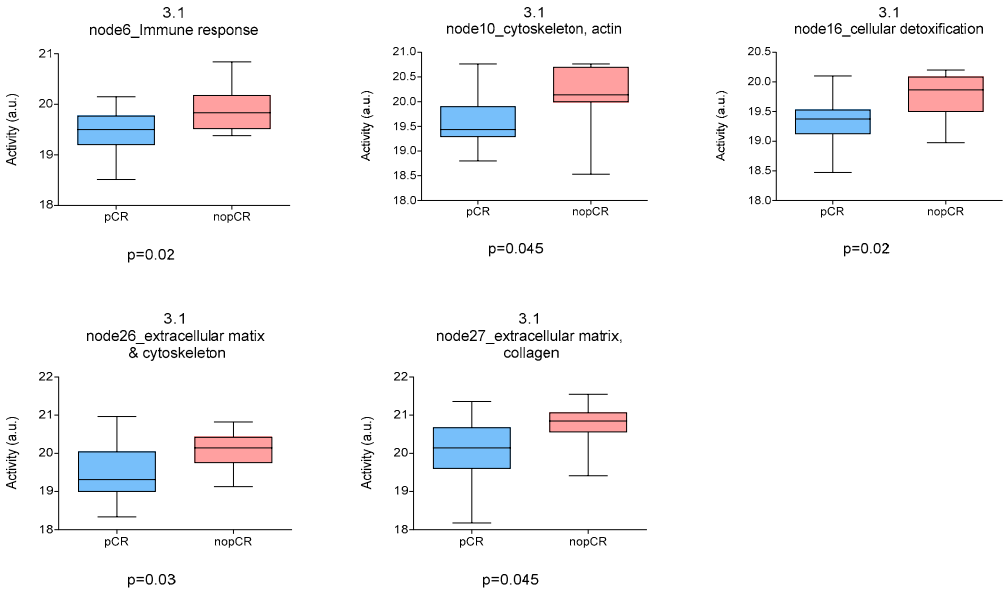


Sup Figure 7: Expression of luminal and basal biomarkers in Layer3 groups in EPIC-MIBC TURBT samples.

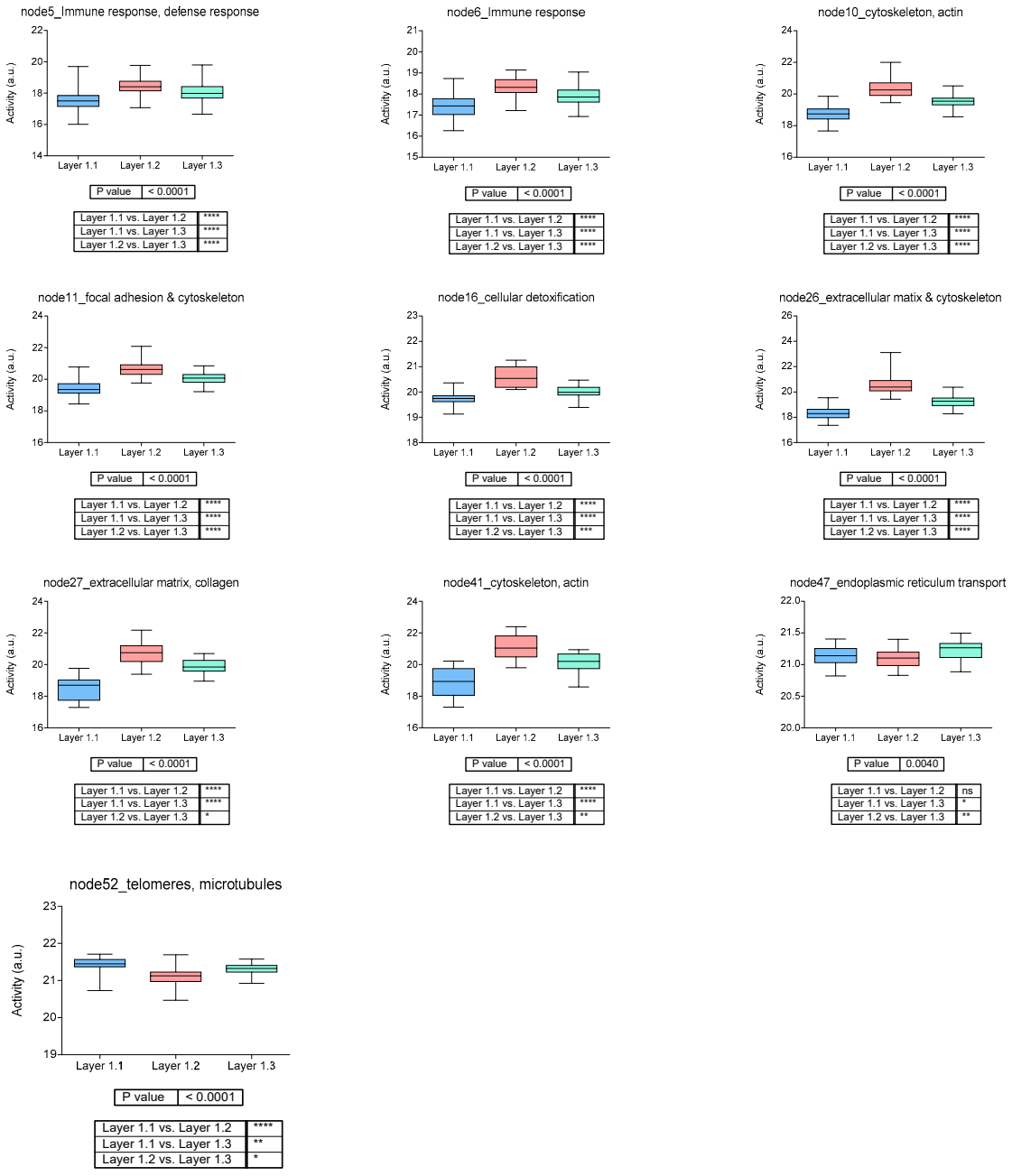


Hazard Ratio (logrank)	A/B	B/A
Ratio (and its reciprocal)	0.3923	2.549
95% CI of ratio	0.1518 to 1.277	0.7829 to 6.588

Sup Fig 8: Disease-free survival in each Layer classification.

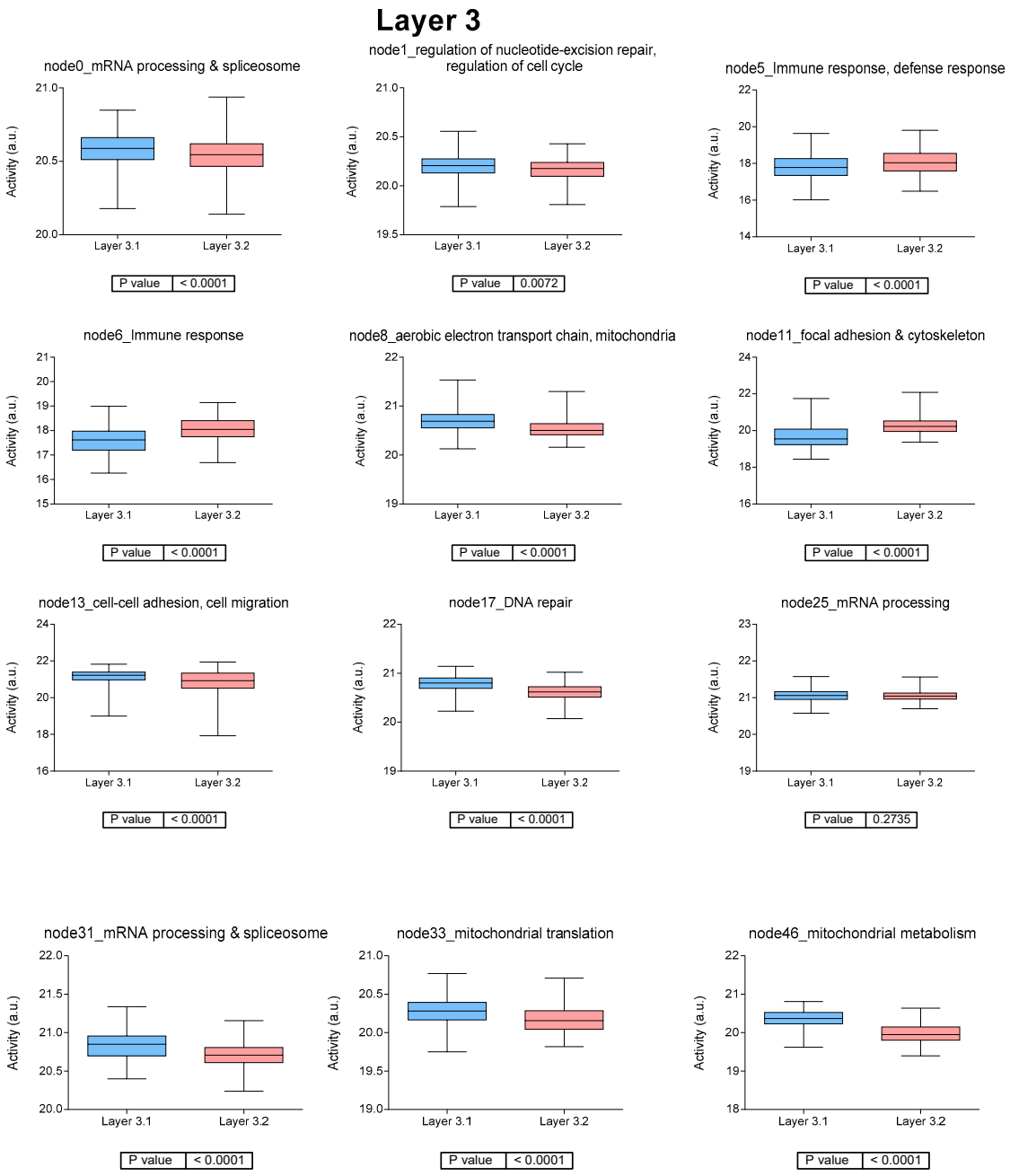


Sup Fig 9: Differential functional node activities according to response to NACT in samples from Layer3.1 group, which includes Luminal tumors.



Sup Fig 10: Differential functional node activities in BLA-TCGA cohort according to Layer1 groups.

being more frequent in Layer1.1 and Layer3.1 (Fig 6).



Sup Fig 11: Differential functional node activities in BLA-TCGA cohort according to Layer3 groups.