**Table S1 GO terms for CDK4/6i differentially expressed genes in the endothelial cluster.**

| **Endothelial cluster \| CDK4/6i downregulated genes \| GO Biological Process** | | | | |
|---|---|---|---|---|
| Name | p-value | adjusted p-value | z score | combined score |
| ribosomal small subunit export from nucleus (GO:0000056) | 0.00698 | 0.05914 | -4.17 | 20.7 |
| mitochondrial ATP synthesis coupled proton transport (GO:0042776) | 0.02178 | 0.07542 | -4.96 | 18.99 |
| mitochondrial electron transport, NADH to ubiquinone (GO:0006120) | 0.001 | 0.04224 | -2.73 | 18.88 |
| mitochondrial ATP synthesis coupled electron transport (GO:0042775) | 8.3E-05 | 0.006288 | -1.9 | 17.87 |
| viral process (GO:0016032) | 6.1E-05 | 0.006288 | -1.7 | 16.45 |
| response to type I interferon (GO:0034340) | 0.00797 | 0.05914 | -2.97 | 14.36 |
| positive regulation of apoptotic cell clearance (GO:2000427) | 0.00797 | 0.05914 | -2.78 | 13.42 |
| ribosomal subunit export from nucleus (GO:0000054) | 0.01293 | 0.06483 | -3.08 | 13.38 |
| regulation of glial cell apoptotic process (GO:0034350) | 0.00698 | 0.05914 | -2.65 | 13.17 |
| positive regulation of nitric-oxide synthase biosynthetic process (GO:0051770) | 0.00996 | 0.06483 | -2.79 | 12.84 |

**Table S2 GO terms for CDK4/6i differentially expressed genes in the HPC cluster.**

**HPC cluster | CDK4/6i downregulated genes | GO Biological Process**

| Name | p-value | adjusted p-value | z score | combined score |
|---|---|---|---|---|
| mitochondrial electron transport, NADH to ubiquinone (GO:0006120) | 2.75E-07 | 0.00001807 | -2.73 | 41.3 |
| mitochondrial ATP synthesis coupled electron transport (GO:0042775) | 6.70E-10 | 1.62E-07 | -1.9 | 40.19 |
| DNA topological change (GO:0006265) | 1.81E-07 | 0.00001588 | -2.48 | 38.54 |
| V(D)J recombination (GO:0033151) | 0.00003847 | 0.0008432 | -3.28 | 33.34 |
| respiratory electron transport chain (GO:0022904) | 1.23E-09 | 1.62E-07 | -1.36 | 27.89 |
| DNA ligation (GO:0006266) | 0.000001453 | 0.00004245 | -2.07 | 27.79 |
| apoptotic nuclear changes (GO:0030262) | 0.000003022 | 0.00007949 | -1.91 | 24.29 |
| DNA ligation involved in DNA repair (GO:0051103) | 0.0001068 | 0.00216 | -2.5 | 22.89 |
| mitochondrial respiratory chain complex I biogenesis (GO:0097031) | 0.000001028 | 0.00003862 | -1.58 | 21.76 |
| NADH dehydrogenase complex assembly (GO:0010257) | 0.000001028 | 0.00003862 | -1.57 | 21.7 |

**HPC cluster | CDK4/6i upregulated genes | GO Biological Process**

| Name | p-value | adjusted p-value | z score | combined score |
|---|---|---|---|---|
| regulated exocytosis (GO:0045055) | 0.00002208 | 0.001921 | -2.3 | 24.7 |
| membrane raft assembly (GO:0001765) | 0.002797 | 0.03577 | -3.89 | 22.88 |
| defense response to protozoan (GO:0042832) | 0.003595 | 0.03577 | -2.98 | 16.76 |
| platelet degranulation (GO:0002576) | 0.00001305 | 0.001921 | -1.44 | 16.15 |
| membrane raft organization (GO:0031579) | 0.004392 | 0.03577 | -2.96 | 16.05 |
| regulation of MHC class II biosynthetic process (GO:0045346) | 0.003595 | 0.03577 | -2.73 | 15.38 |
| positive regulation of cAMP-mediated signaling (GO:0043950) | 0.003595 | 0.03577 | -2.7 | 15.2 |
| positive regulation of macrophage differentiation (GO:0045651) | 0.003595 | 0.03577 | -2.59 | 14.56 |
| genetic imprinting (GO:0071514) | 0.003595 | 0.03577 | -2.57 | 14.45 |
| regulation of glycogen (starch) synthase activity (GO:2000465) | 0.003196 | 0.03577 | -2.44 | 14.04 |

**Table S3 GO terms for CDK4/6i differentially expressed genes in the erythroid cluster.**

| **Erythroid cluster \| CDK4/6i downregulated genes \| GO Biological Process** | | | | |
|---|---|---|---|---|
| Name | p-value | adjusted p-value | z score | combined score |
| mitochondrial ATP synthesis coupled electron transport (GO:0042775) | 2.92E-10 | 1.25E-07 | -1.9 | 41.77 |
| mitochondrial electron transport, NADH to ubiquinone (GO:0006120) | 0.000002073 | 0.0002228 | -2.73 | 35.77 |
| V(D)J recombination (GO:0033151) | 0.000103 | 0.00492 | -3.28 | 30.13 |
| respiratory electron transport chain (GO:0022904) | 5.92E-10 | 1.27E-07 | -1.36 | 28.88 |
| mitochondrial respiratory chain complex assembly (GO:0033108) | 0.000001286 | 0.0001843 | -1.78 | 24.16 |
| DNA topological change (GO:0006265) | 0.0001651 | 0.007099 | -2.47 | 21.54 |
| DNA geometric change (GO:0032392) | 0.00001531 | 0.0008227 | -1.87 | 20.72 |
| DNA ligation involved in DNA repair (GO:0051103) | 0.0002851 | 0.009431 | -2.5 | 20.44 |
| mitochondrial respiratory chain complex I biogenesis (GO:0097031) | 0.000007671 | 0.0004712 | -1.58 | 18.59 |
| NADH dehydrogenase complex assembly (GO:0010257) | 0.000007671 | 0.0004712 | -1.57 | 18.54 |

| **Erythroid cluster \| CDK4/6i upregulated genes \| GO Biological Process** | | | | |
|---|---|---|---|---|
| Name | p-value | adjusted p-value | z score | combined score |
| membrane raft assembly (GO:0001765) | 0.004193 | 0.05535 | -3.89 | 21.31 |
| regulation of viral entry into host cell (GO:0046596) | 0.0001149 | 0.02343 | -1.89 | 17.14 |
| regulation of muscle system process (GO:0090257) | 0.005985 | 0.05535 | -2.94 | 15.05 |
| membrane raft organization (GO:0031579) | 0.006582 | 0.05535 | -2.96 | 14.86 |
| genetic imprinting (GO:0071514) | 0.005388 | 0.05535 | -2.57 | 13.41 |
| response to muscle stretch (GO:0035994) | 0.005985 | 0.05535 | -2.57 | 13.14 |
| regulation of glycogen (starch) synthase activity (GO:2000465) | 0.004791 | 0.05535 | -2.44 | 13.05 |
| negative regulation of DNA metabolic process (GO:0051053) | 0.0003079 | 0.0314 | -1.52 | 12.28 |
| regulation of apoptotic process (GO:0042981) | 0.001047 | 0.05535 | -1.79 | 12.27 |
| positive regulation of G1/S transition of mitotic cell cycle (GO:1900087) | 0.01016 | 0.05535 | -2.66 | 12.22 |

**Table S4 GO terms for CDK4/6i differentially expressed genes in the mesenchymal cluster.**

| **Mesenchymal cluster \| CDK4/6i downregulated genes \| GO Biological Process** | | | | |
|---|---|---|---|---|
| Name | p-value | adjusted p-value | z score | combined score |
| mitochondrial electron transport, NADH to ubiquinone (GO:0006120) | 0.000009682 | 0.000568 | -2.74 | 31.58 |
| mitochondrial ATP synthesis coupled electron transport (GO:0042775) | 9.31E-07 | 0.0001222 | -1.9 | 26.42 |
| ribosomal small subunit export from nucleus (GO:0000056) | 0.006284 | 0.04096 | -4.16 | 21.09 |
| mitochondrial ATP synthesis coupled proton transport (GO:0042776) | 0.01962 | 0.05571 | -4.94 | 19.43 |
| respiratory electron transport chain (GO:0022904) | 0.000001389 | 0.0001222 | -1.36 | 18.33 |
| mitochondrial respiratory chain complex I biogenesis (GO:0097031) | 0.00002582 | 0.0007574 | -1.58 | 16.68 |
| NADH dehydrogenase complex assembly (GO:0010257) | 0.00002582 | 0.0007574 | -1.57 | 16.64 |
| mitochondrial respiratory chain complex assembly (GO:0033108) | 0.00008825 | 0.002219 | -1.78 | 16.58 |
| V(D)J recombination (GO:0033151) | 0.007179 | 0.04211 | -3.26 | 16.12 |
| mitochondrial respiratory chain complex I assembly (GO:0032981) | 0.00002582 | 0.0007574 | -1.41 | 14.9 |

**Table S5 GO terms for CDK1i differentially expressed genes in the endothelial cluster.**

**Endothelial cluster | CDK1i downregulated genes | GO Biological Process**

| Name | p-value | adjusted p-value | z score | combined score |
|---|---|---|---|---|
| positive regulation of nitric-oxide synthase biosynthetic process (GO:0051770) | 0.0000383 | 0.01255 | -2.82 | 28.65 |
| regulation of nitric-oxide synthase biosynthetic process (GO:0051769) | 0.00006628 | 0.01255 | -2.58 | 24.83 |
| ribosomal small subunit export from nucleus (GO:0000056) | 0.006632 | 0.05774 | -4.15 | 20.81 |
| mitochondrial ATP synthesis coupled proton transport (GO:0042776) | 0.0207 | 0.05998 | -4.86 | 18.84 |
| positive regulation of activated T cell proliferation (GO:0042104) | 0.0001608 | 0.01267 | -2.15 | 18.76 |
| positive regulation of cell migration by vascular endothelial growth factor signaling pathway (GO:0038089) | 0.007576 | 0.05774 | -3.47 | 16.95 |
| regulation of positive chemotaxis (GO:0050926) | 0.008519 | 0.05774 | -3.55 | 16.93 |
| protein kinase B signaling (GO:0043491) | 0.0005284 | 0.02313 | -1.97 | 14.87 |
| response to type I interferon (GO:0034340) | 0.007576 | 0.05774 | -2.95 | 14.4 |
| positive regulation of apoptotic cell clearance (GO:2000427) | 0.007576 | 0.05774 | -2.76 | 13.47 |

**Endothelial cluster | CDK1i upregulated genes | GO Biological Process**

| Name | p-value | adjusted p-value | z score | combined score |
|---|---|---|---|---|
| cytoskeleton-dependent intracellular transport (GO:0030705) | 0.00007845 | 0.006058 | -2.09 | 19.73 |
| regulation of transcription from RNA polymerase II promoter in response to oxidative stress (GO:0043619) | 0.004492 | 0.04395 | -3.6 | 19.45 |
| cell cycle G2/M phase transition (GO:0044839) | 0.00002973 | 0.005055 | -1.82 | 18.98 |
| V(D)J recombination (GO:0033151) | 0.003994 | 0.04395 | -3.27 | 18.05 |
| regulation of mitotic cell cycle phase transition (GO:1901990) | 0.00008908 | 0.006058 | -1.91 | 17.85 |
| outer mitochondrial membrane organization (GO:0007008) | 0.003994 | 0.04395 | -3.23 | 17.84 |
| regulation of G2/M transition of mitotic cell cycle (GO:0010389) | 0.00004774 | 0.005411 | -1.77 | 17.61 |
| negative regulation of translation in response to stress (GO:0032055) | 0.003495 | 0.04395 | -3.09 | 17.48 |
| regulation of translational initiation in response to stress (GO:0043558) | 0.003495 | 0.04395 | -2.84 | 16.07 |
| regulation of nuclease activity (GO:0032069) | 0.003495 | 0.04395 | -2.83 | 15.99 |

**Table S6 GO terms for CDK1i differentially expressed genes in the HPC cluster.**

| **HPC cluster \| CDK1i downregulated genes \| GO Biological Process** | | | | |
|---|---|---|---|---|
| Name | p-value | adjusted p-value | z score | combined score |
| mitochondrial ATP synthesis coupled electron transport (GO:0042775) | 8.30E-11 | 4.67E-08 | -1.9 | 44.16 |
| mitochondrial electron transport, NADH to ubiquinone (GO:0006120) | 0.000001458 | 0.0001368 | -2.73 | 36.68 |
| respiratory electron transport chain (GO:0022904) | 2.06E-10 | 5.79E-08 | -1.36 | 30.32 |
| mitochondrial ATP synthesis coupled proton transport (GO:0042776) | 0.003724 | 0.03913 | -4.95 | 27.71 |
| mitochondrial electron transport, cytochrome c to oxygen (GO:0006123) | 0.0001003 | 0.002822 | -2.57 | 23.62 |
| mRNA splicing, via spliceosome (GO:0000398) | 0.000001398 | 0.0001368 | -1.75 | 23.54 |
| histone mRNA metabolic process (GO:0008334) | 0.0001484 | 0.003632 | -2.29 | 20.16 |
| gene expression (GO:0010467) | 1.29E-07 | 0.00002419 | -1.26 | 19.94 |
| establishment of protein localization to mitochondrion (GO:0072655) | 0.00005491 | 0.001932 | -2.02 | 19.86 |
| nucleocytoplasmic transport (GO:0006913) | 0.00004293 | 0.001859 | -1.95 | 19.59 |

| **HPC cluster \| CDK1i upregulated genes \| GO Biological Process** | | | | |
|---|---|---|---|---|
| Name | p-value | adjusted p-value | z score | combined score |
| cellular iron ion homeostasis (GO:0006879) | 0.000003262 | 0.0008498 | -2.65 | 33.52 |
| iron ion homeostasis (GO:0055072) | 9.99E-08 | 0.00005206 | -1.57 | 25.36 |
| oxygen homeostasis (GO:0032364) | 0.01253 | 0.09524 | -4.65 | 20.36 |
| positive regulation of cell cycle arrest (GO:0071158) | 0.00001468 | 0.001912 | -1.71 | 19.01 |
| ribosomal small subunit export from nucleus (GO:0000056) | 0.01253 | 0.09524 | -4.12 | 18.06 |
| gas homeostasis (GO:0033483) | 0.01431 | 0.09524 | -4.11 | 17.47 |
| neutrophil degranulation (GO:0043312) | 0.0001957 | 0.01014 | -2.01 | 17.14 |
| cellular transition metal ion homeostasis (GO:0046916) | 0.00002402 | 0.002503 | -1.59 | 16.88 |
| neutrophil mediated immunity (GO:0002446) | 0.000214 | 0.01014 | -1.93 | 16.31 |
| DNA damage response, signal transduction by p53 class mediator (GO:0030330) | 0.00001468 | 0.001912 | -1.42 | 15.84 |

**Table S7 GO terms for CDK1i differentially expressed genes in the erythroid cluster.**

<table>
<tr><th colspan="5">Erythroid cluster | CDK1i downregulated genes | GO Biological Process</th></tr>
<tr><th>Name</th><th>p-value</th><th>adjusted p-value</th><th>z score</th><th>combined score</th></tr>
<tr><td>regulation of protein targeting (GO:1903533)</td><td>0.005936</td><td>0.03332</td><td>-4.26</td><td>21.86</td></tr>
<tr><td>ribosomal small subunit export from nucleus (GO:0000056)</td><td>0.005936</td><td>0.03332</td><td>-4.17</td><td>21.37</td></tr>
<tr><td>mitochondrial electron transport, NADH to ubiquinone (GO:0006120)</td><td>0.0007188</td><td>0.02581</td><td>-2.74</td><td>19.8</td></tr>
<tr><td>mitochondrial ATP synthesis coupled proton transport (GO:0042776)</td><td>0.01854</td><td>0.04191</td><td>-4.96</td><td>19.77</td></tr>
<tr><td>mitochondrial ATP synthesis coupled electron transport (GO:0042775)</td><td>0.00004997</td><td>0.003801</td><td>-1.9</td><td>18.84</td></tr>
<tr><td>folic acid-containing compound biosynthetic process (GO:0009396)</td><td>0.005936</td><td>0.03332</td><td>-3.45</td><td>17.69</td></tr>
<tr><td>oxygen transport (GO:0015671)</td><td>0.006781</td><td>0.03332</td><td>-3.32</td><td>16.57</td></tr>
<tr><td>positive regulation of autophagy of mitochondrion (GO:1903599)</td><td>0.006781</td><td>0.03332</td><td>-3</td><td>15</td></tr>
<tr><td>ribosomal subunit export from nucleus (GO:0000054)</td><td>0.011</td><td>0.04056</td><td>-3.08</td><td>13.89</td></tr>
<tr><td>pteridine-containing compound biosynthetic process (GO:0042559)</td><td>0.006781</td><td>0.03332</td><td>-2.68</td><td>13.41</td></tr>
<tr><th colspan="5">Erythroid cluster | CDK1i upregulated genes | GO Biological Process</th></tr>
<tr><th>Name</th><th>p-value</th><th>adjusted p-value</th><th>z score</th><th>combined score</th></tr>
<tr><td>negative regulation of membrane protein ectodomain proteolysis (GO:0051045)</td><td>0.003196</td><td>0.04232</td><td>-2.66</td><td>15.26</td></tr>
<tr><td>negative regulation of reproductive process (GO:2000242)</td><td>0.004392</td><td>0.04232</td><td>-2.54</td><td>13.81</td></tr>
<tr><td>sequestering of actin monomers (GO:0042989)</td><td>0.004392</td><td>0.04232</td><td>-2.43</td><td>13.17</td></tr>
<tr><td>regulation of integrin-mediated signaling pathway (GO:2001044)</td><td>0.004791</td><td>0.04232</td><td>-2.3</td><td>12.27</td></tr>
<tr><td>regulation of trophoblast cell migration (GO:1901163)</td><td>0.004791</td><td>0.04232</td><td>-2.24</td><td>11.96</td></tr>
<tr><td>negative regulation of DNA replication (GO:0008156)</td><td>0.006781</td><td>0.04303</td><td>-2.2</td><td>10.96</td></tr>
<tr><td>positive regulation of viral entry into host cell (GO:0046598)</td><td>0.003595</td><td>0.04232</td><td>-1.85</td><td>10.44</td></tr>
<tr><td>transition metal ion homeostasis (GO:0055076)</td><td>0.009958</td><td>0.04303</td><td>-2.23</td><td>10.26</td></tr>
<tr><td>cellular iron ion homeostasis (GO:0006879)</td><td>0.02258</td><td>0.0497</td><td>-2.61</td><td>9.91</td></tr>
<tr><td>negative regulation of actin filament polymerization (GO:0030837)</td><td>0.009165</td><td>0.04303</td><td>-1.83</td><td>8.57</td></tr>
</table>

**Table S8 GO terms for CDK1i differentially expressed genes in the mesenchymal cluster.**

| **Mesenchymal cluster \| CDK1i downregulated genes \| GO Biological Process** | | | | |
|---|---|---|---|---|
| Name | p-value | adjusted p-value | z score | combined score |
| ribosomal small subunit export from nucleus (GO:0000056) | 0.005587 | 0.0459 | -4.17 | 21.63 |
| mitochondrial electron transport, NADH to ubiquinone (GO:0006120) | 0.0006352 | 0.0305 | -2.74 | 20.14 |
| mitochondrial ATP synthesis coupled proton transport (GO:0042776) | 0.01746 | 0.05732 | -4.96 | 20.08 |
| mitochondrial ATP synthesis coupled electron transport (GO:0042775) | 0.00004128 | 0.004197 | -1.9 | 19.21 |
| bleb assembly (GO:0032060) | 0.006383 | 0.0459 | -3 | 15.15 |
| ribosomal subunit export from nucleus (GO:0000054) | 0.01035 | 0.05579 | -3.08 | 14.08 |
| respiratory electron transport chain (GO:0022904) | 0.00005559 | 0.004197 | -1.36 | 13.32 |
| genetic imprinting (GO:0071514) | 0.007178 | 0.04927 | -2.56 | 12.64 |
| regulation of glycogen (starch) synthase activity (GO:2000465) | 0.006383 | 0.0459 | -2.43 | 12.27 |
| protein targeting to ER (GO:0045047) | 0.002727 | 0.03956 | -2.08 | 12.26 |