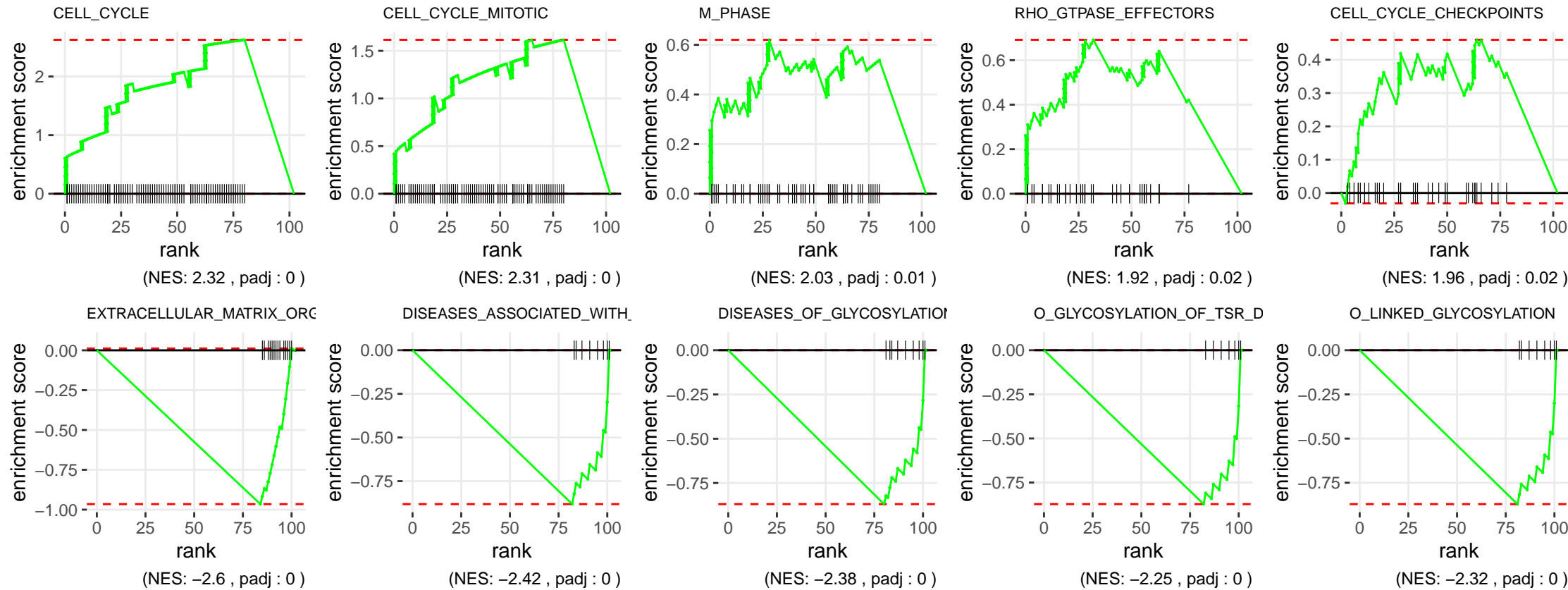












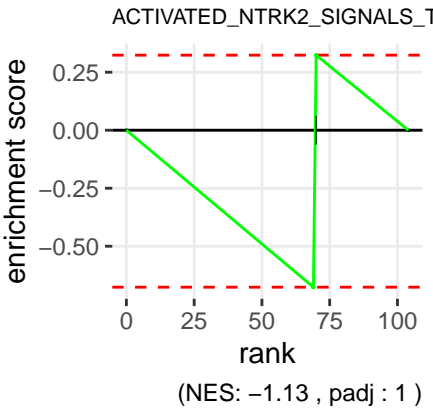
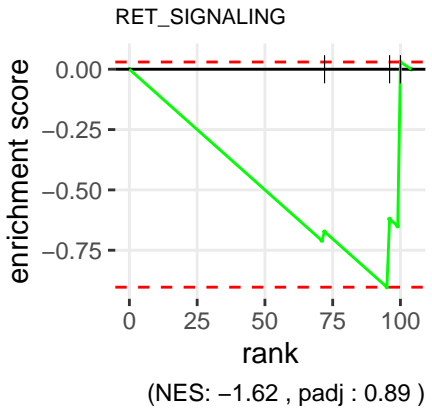
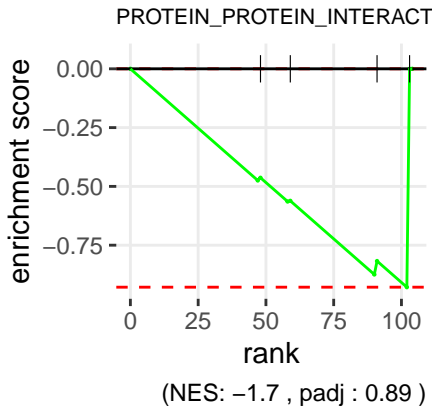
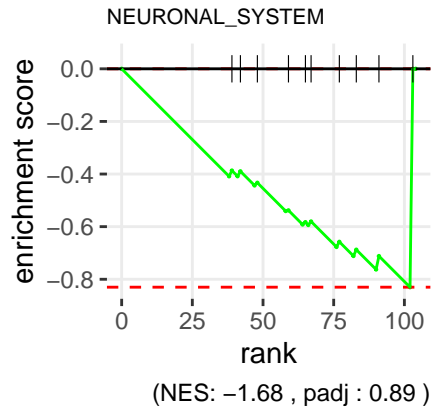
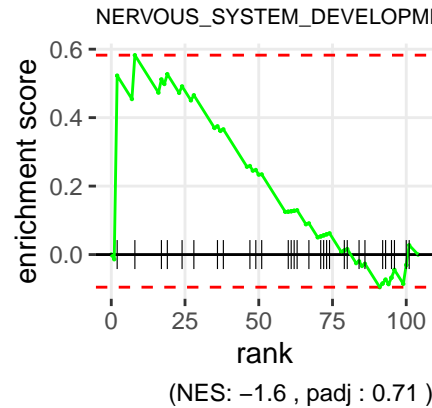
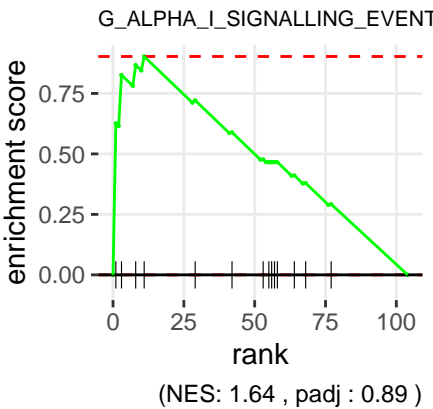
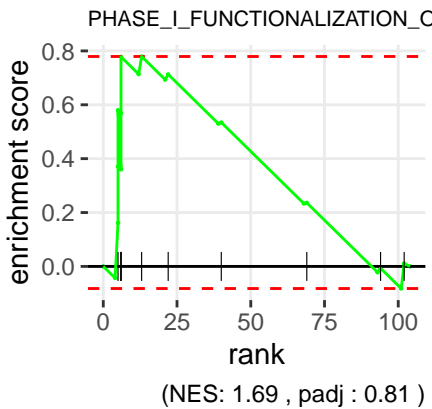
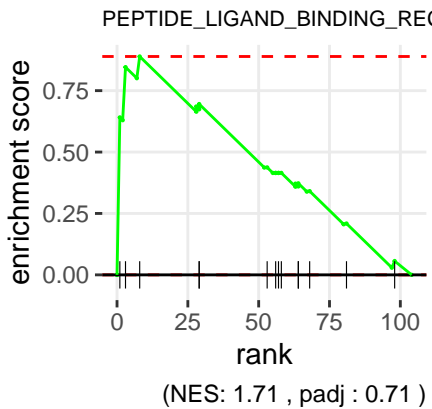
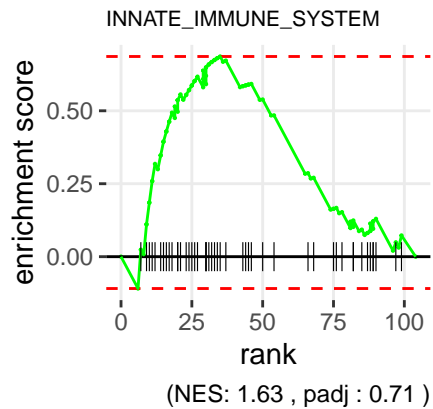
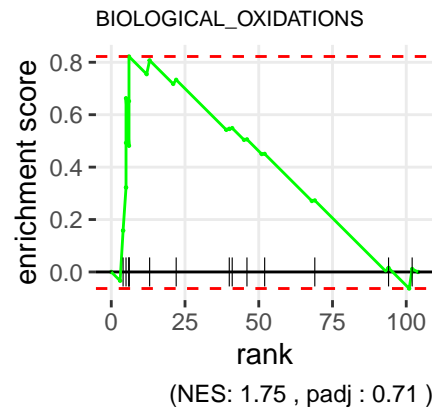
D4 ECs : Top enriched Pathways (GSEA), Old vs Young

| Pathway | Gene ranks | NES | pval | padj |
|---|------------|-------|---------|---------|
| REACTOME_CELL_CYCLE | | 2.32 | 1.0e-09 | 6.5e-07 |
| REACTOME_CELL_CYCLE_MITOTIC | | 2.31 | 5.3e-09 | 1.6e-06 |
| REACTOME_M_PHASE | | 2.03 | 8.1e-05 | 5.0e-03 |
| REACTOME_RHO_GTPASE_EFFECTORS | | 1.92 | 3.6e-04 | 2.0e-02 |
| REACTOME_CELL_CYCLE_CHECKPOINTS | | 1.96 | 3.9e-04 | 2.0e-02 |
| REACTOME_O_LINKED_GLYCOSYLATION | | -2.32 | 5.8e-06 | 5.1e-04 |
| REACTOME_O_GLYCOSYLATION_OF_TSR_DOMAIN_CONTAINING_PROTEINS | | -2.25 | 2.1e-06 | 2.2e-04 |
| REACTOME_DISEASES_OF_GLYCOSYLATION | | -2.38 | 1.7e-06 | 2.1e-04 |
| REACTOME_DISEASES_ASSOCIATED_WITH_O_GLYCOSYLATION_OF_PROTEINS | | -2.42 | 9.3e-07 | 1.4e-04 |
| REACTOME_EXTRACELLULAR_MATRIX_ORGANIZATION | | -2.60 | 2.3e-08 | 4.7e-06 |



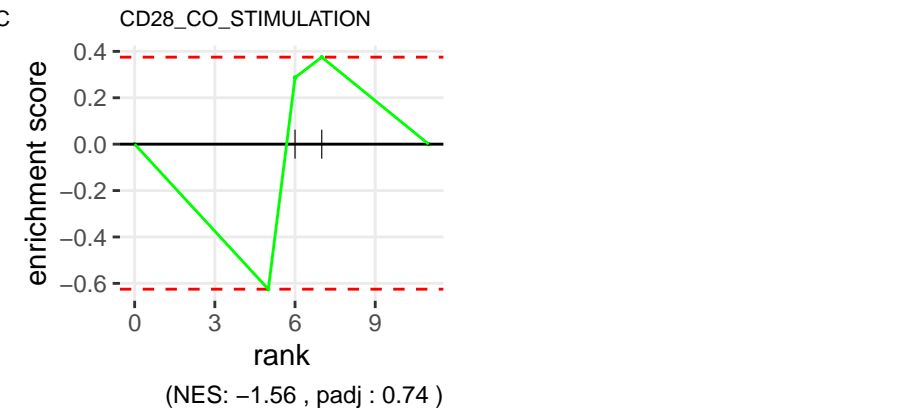
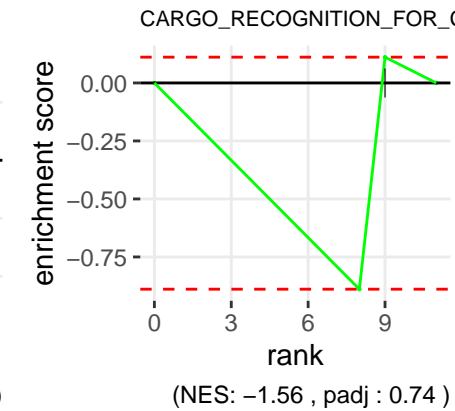
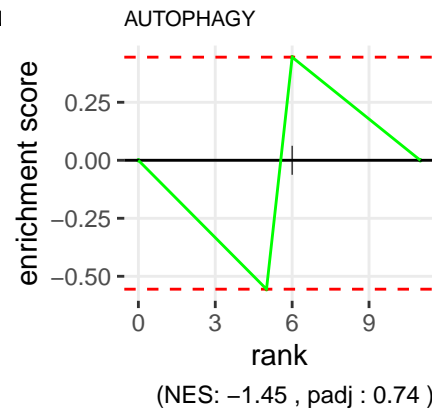
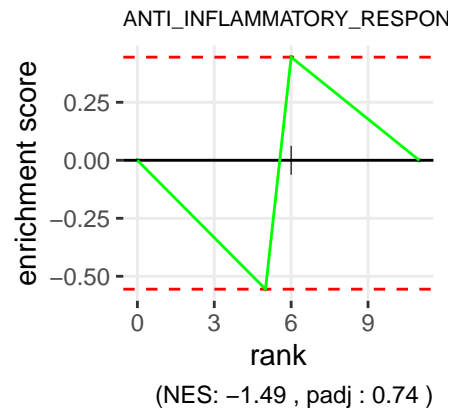
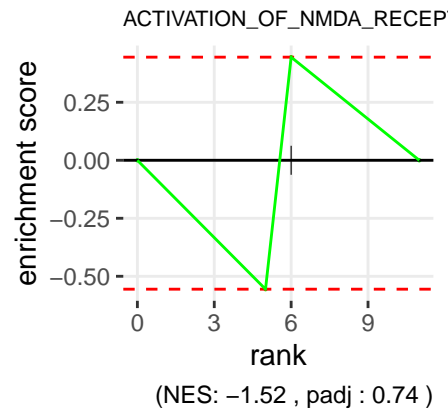
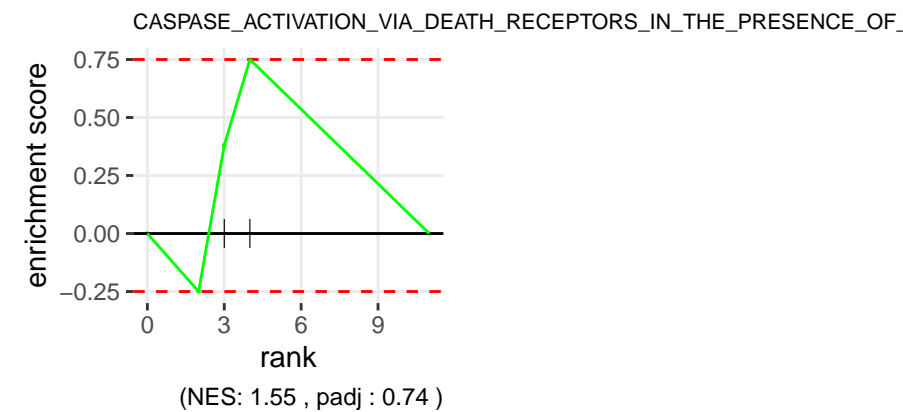
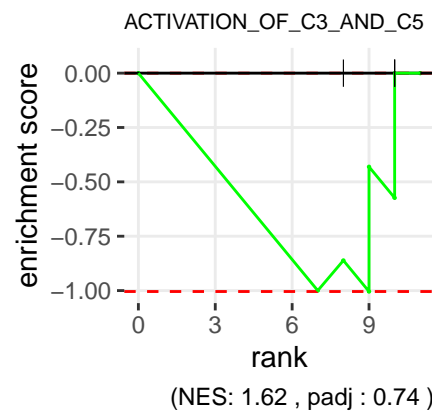
D4 FAPs : Top enriched Pathways (GSEA), Old vs Young

| Pathway | Gene ranks | NES | pval | padj |
|---|---|-------|---------|---------|
| REACTOME_BIOLOGICAL_OXIDATIONS |  | 1.75 | 3.4e-03 | 7.1e-01 |
| REACTOME_INNATE_IMMUNE_SYSTEM |  | 1.63 | 6.1e-03 | 7.1e-01 |
| REACTOME_PEPTIDE_LIGAND_BINDING_RECEPTORS |  | 1.71 | 5.6e-03 | 7.1e-01 |
| REACTOME_PHASE_I_FUNCTIONALIZATION_OF_COMPOUNDS |  | 1.69 | 8.6e-03 | 8.1e-01 |
| REACTOME_G_ALPHA_I_SIGNALLING_EVENTS |  | 1.64 | 1.7e-02 | 8.9e-01 |
| REACTOME_ACTIVATED_NTRK2_SIGNALS_THROUGH_CDK5 |  | -1.13 | 3.6e-01 | 1.0e+00 |
| REACTOME_RET_SIGNALING |  | -1.62 | 1.6e-02 | 8.9e-01 |
| REACTOME_PROTEIN_PROTEIN_INTERACTIONS_AT_SYNAPSES |  | -1.70 | 1.7e-02 | 8.9e-01 |
| REACTOME_NEURONAL_SYSTEM |  | -1.68 | 1.6e-02 | 8.9e-01 |
| REACTOME_NERVOUS_SYSTEM_DEVELOPMENT |  | -1.60 | 3.9e-03 | 7.1e-01 |

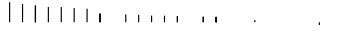

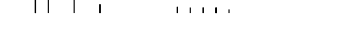









D4 M1 : Top enriched Pathways (GSEA), Old vs Young

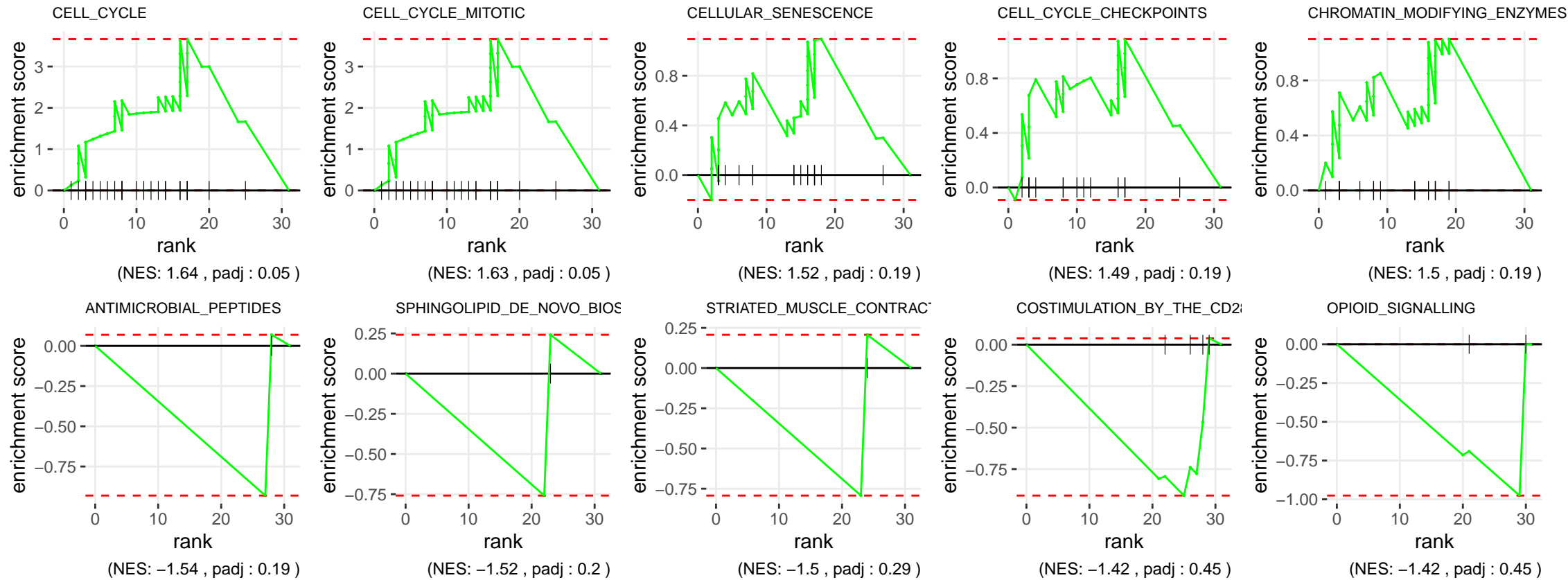
| Pathway | Gene ranks | NES | pval | padj |
|--|------------|-------|---------|---------|
| PKIN1_STIMULATES_TRANSCRIPTION_OF_AR_ANDROGEN_RECEPTOR_REGULATED_GENES_KLK2_AND_KLK3 | | 1.49 | 1.6e-01 | 7.4e-01 |
| ACTIVATION_OF_ANTERIOR_HOX_GENES_IN_HINDBRAIN_DEVELOPMENT_DURING_EARLY_EMBRYOGENESIS | | 1.51 | 1.6e-01 | 7.4e-01 |
| REACTOME_ACTIVATION_OF_C3_AND_C5 | | 1.62 | 1.1e-01 | 7.4e-01 |
| REACTOME_B_WICH_COMPLEX_POSITIVELY_REGULATES_RRNA_EXPRESSION | | 1.51 | 1.6e-01 | 7.4e-01 |
| REACTOME_CASPASE_ACTIVATION_VIA_DEATH_RECEPTORS_IN_THE_PRESENCE_OF_LIGAND | | 1.55 | 1.4e-01 | 7.4e-01 |
| REACTOME_CD28_CO_STIMULATION | | -1.56 | 1.6e-01 | 7.4e-01 |
| REACTOME_CARGO_RECOGNITION_FOR_CLATHRIN_MEDIATED_ENDOCYTOSIS | | -1.56 | 7.9e-02 | 7.4e-01 |
| REACTOME_AUTOPHAGY | | -1.45 | 1.7e-01 | 7.4e-01 |
| REACTOME_ANTI_INFLAMMATORY_RESPONSE_FAVOURING_LEISHMANIA_PARASITE_INFECTION | | -1.49 | 1.3e-01 | 7.4e-01 |
| REACTOME_ACTIVATION_OF_NMDA_RECEPTORS_AND_POSTSYNAPTIC_EVENTS | | -1.52 | 1.3e-01 | 7.4e-01 |





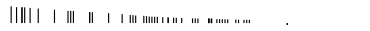

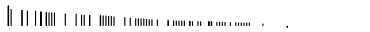
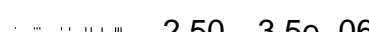
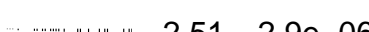



D4 M2 : Top enriched Pathways (GSEA), Old vs Young

| Pathway | Gene ranks | NES | pval | padj |
|--|---|-------|---------|---------|
| REACTOME_CELL_CYCLE |  | 1.64 | 1.6e-04 | 4.9e-02 |
| REACTOME_CELL_CYCLE_MITOTIC |  | 1.63 | 1.2e-04 | 4.9e-02 |
| REACTOME_CELLULAR_SENESCENCE |  | 1.52 | 2.4e-03 | 1.9e-01 |
| REACTOME_CELL_CYCLE_CHECKPOINTS |  | 1.49 | 3.5e-03 | 1.9e-01 |
| REACTOME_CHROMATIN_MODIFYING_ENZYMES |  | 1.50 | 5.8e-03 | 1.9e-01 |
| REACTOME_OPIOID_SIGNALLING |  | -1.42 | 6.4e-02 | 4.5e-01 |
| REACTOME_COSTIMULATION_BY_THE_CD28_FAMILY |  | -1.42 | 6.9e-02 | 4.5e-01 |
| REACTOME_STRIATED_MUSCLE_CONTRACTION |  | -1.50 | 3.4e-02 | 2.9e-01 |
| REACTOME_SPHINGOLIPID_DE_NOVO_BIOSYNTHESIS |  | -1.52 | 1.6e-02 | 2.0e-01 |
| REACTOME_ANTIMICROBIAL_PEPTIDES |  | -1.54 | 5.5e-03 | 1.9e-01 |

0 10 20 30



D4 sCs : Top enriched Pathways (GSEA), Old vs Young

| Pathway | Gene ranks | NES | pval | padj |
|--|---|-------|---------|---------|
| REACTOME_CELLULAR_SENESCENCE |  | 3.15 | 1.0e-10 | 1.1e-08 |
| REACTOME_CELL_CYCLE |  | 3.60 | 1.0e-10 | 1.1e-08 |
| REACTOME_CELL_CYCLE_CHECKPOINTS |  | 3.19 | 1.0e-10 | 1.1e-08 |
| REACTOME_CELL_CYCLE_MITOTIC |  | 3.59 | 1.0e-10 | 1.1e-08 |
| REACTOME_M_PHASE |  | 3.18 | 1.0e-10 | 1.1e-08 |
| REACTOME_ELASTIC_FIBRE_FORMATION |  | -2.50 | 3.5e-06 | 4.1e-05 |
| REACTOME_COLLAGEN_FORMATION |  | -2.51 | 2.9e-06 | 3.5e-05 |
| REACTOME_ECM_PROTEOGLYCANs |  | -2.49 | 2.2e-06 | 2.9e-05 |
| REACTOME_DEGRADATION_OF_THE_EXTRACELLULAR_MATRIX |  | -2.56 | 8.2e-07 | 1.3e-05 |
| REACTOME_EXTRACELLULAR_MATRIX_ORGANIZATION |  | -3.02 | 1.0e-10 | 1.1e-08 |
| | 050100 | | | |

