

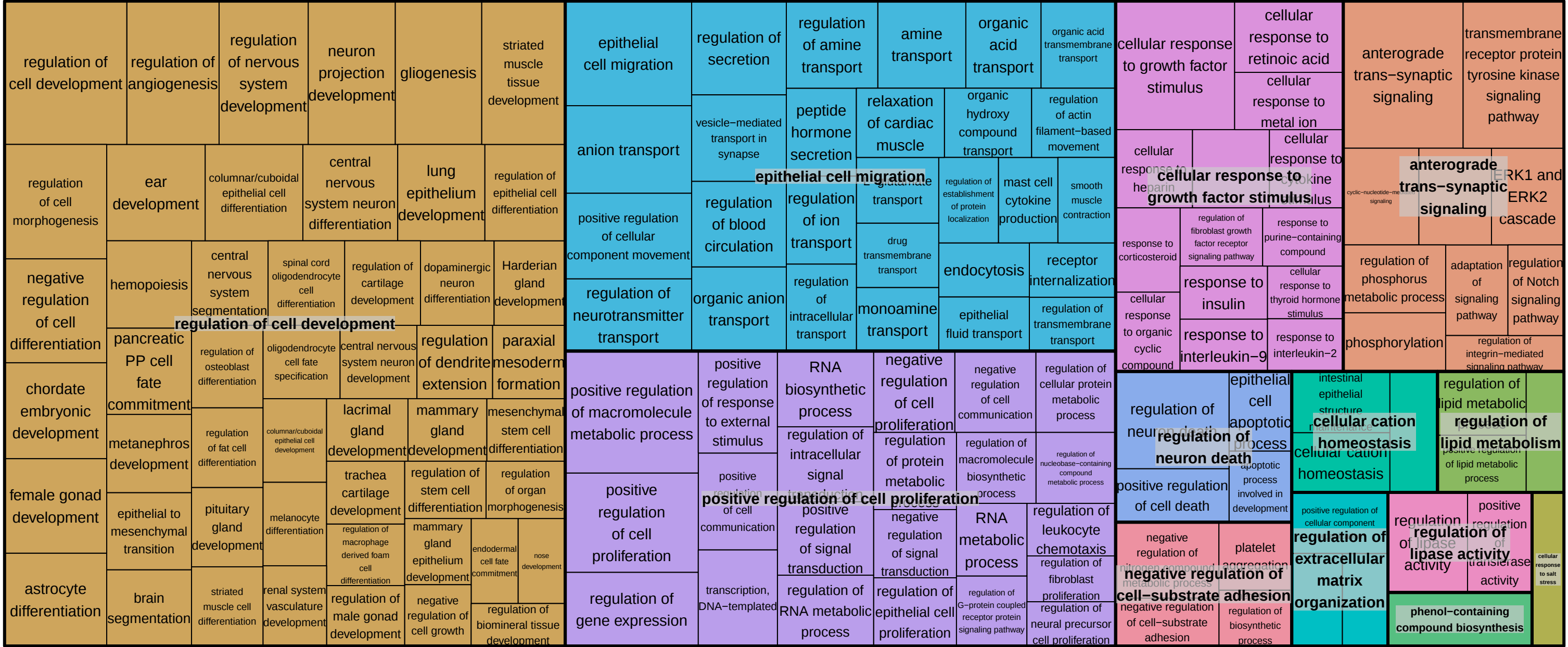
Additional File 5. Complete list of GO terms for essential genes

Common Hypervariable Essential GO Annotations

|                                             |                                                        |                                           |                                               |                                        |                                             |                                             |                           |                                                    |                                    |
|---------------------------------------------|--------------------------------------------------------|-------------------------------------------|-----------------------------------------------|----------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------|----------------------------------------------------|------------------------------------|
| Harderian gland development                 | tongue development                                     | regulation of leukocyte differentiation   | regulation of epithelial cell differentiation | regulation of vasculature development  | cellular response to growth factor stimulus | response to insulin                         | ERK1 and ERK2 cascade     | phosphatidylinositol-mediated signaling            | cellular cation homeostasis        |
| positive regulation of cell differentiation | regulation of epithelial cell proliferation            | skeletal muscle organ development         | striated muscle tissue development            | regulation of myoblast differentiation | cyclic-nucleotide-mediated signaling        | cellular response to growth factor stimulus |                           | cellular response to lipid                         | cellular cation homeostasis        |
| positive regulation of cell proliferation   | eye morphogenesis                                      | positive regulation of cell death         | astrocyte differentiation                     | gliogenesis                            | adaptation of signaling pathway             | response to corticosteroid                  |                           | response to cadmium ion                            | cellular response to retinoic acid |
| smooth muscle cell differentiation          | positive regulation of macromolecule metabolic process |                                           | metanephros development                       |                                        | smooth muscle contraction                   | spermatogenesis                             | epithelial cell migration | positive regulation of cellular component movement | water homeostasis                  |
|                                             |                                                        | negative regulation of cell proliferation |                                               |                                        |                                             |                                             |                           | regulation of blood vessel size                    | carboxylic acid biosynthesis       |



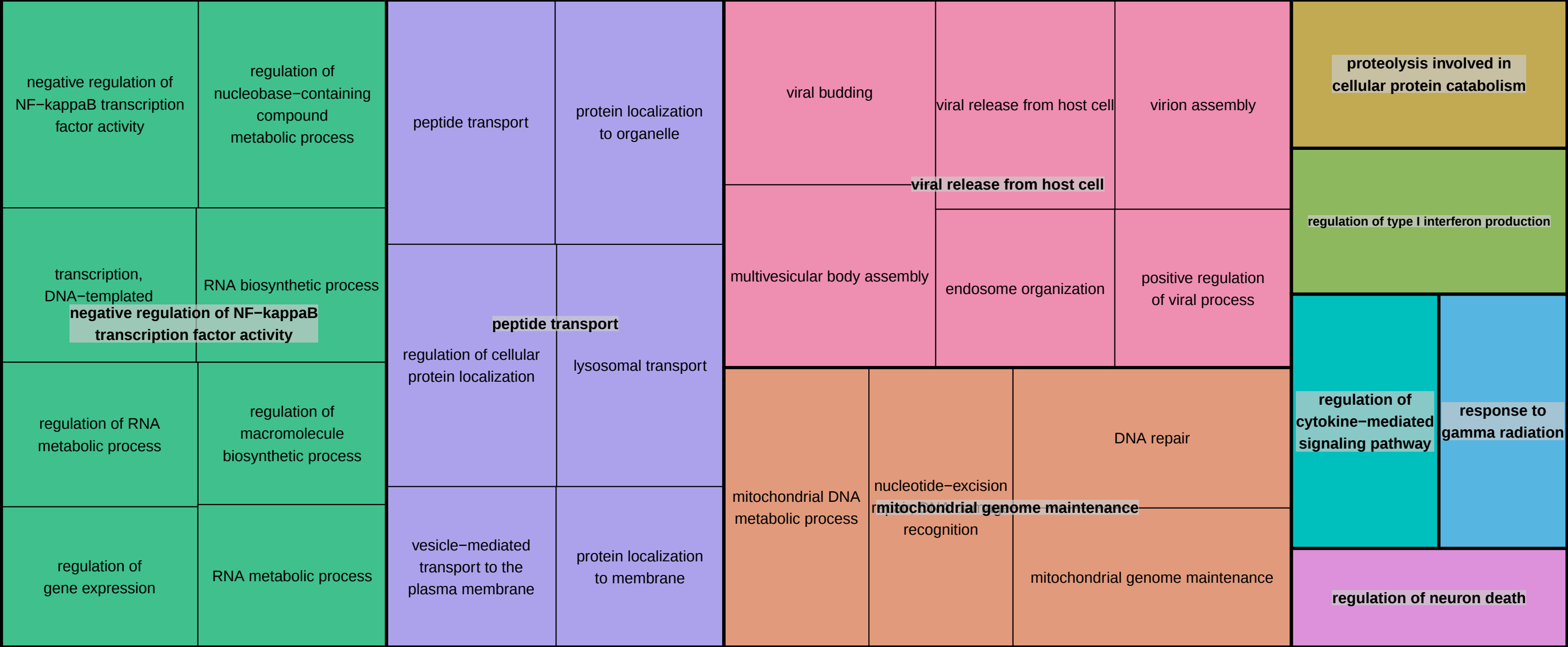
Hypervariable Essential GO Annotations in Cerebellum Tissue



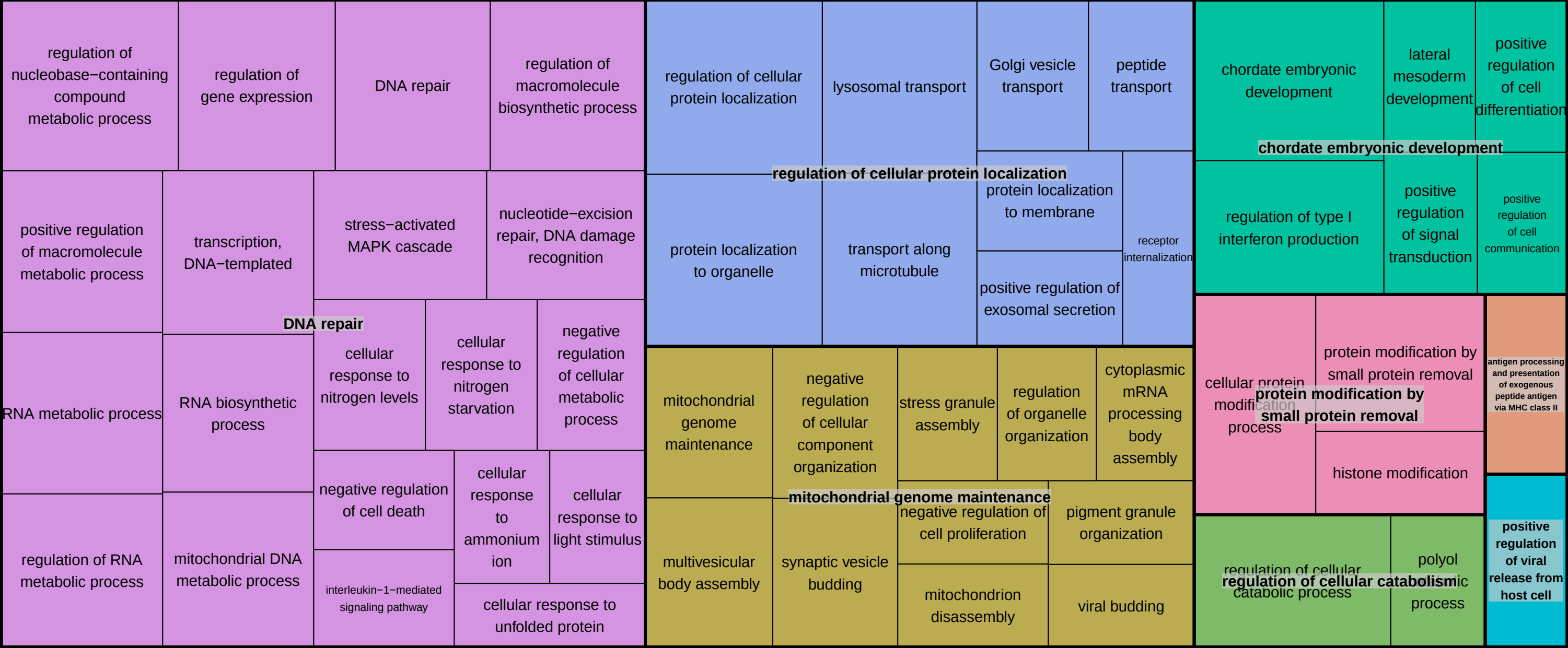
## Hypervariable Essential GO Annotations in Frontal Cortex Tissue

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|--------------------------------------------------------|------------------------------------------------------------|--------------------------------------------------------|--------------------------------------------------|--------------------------------------------------|-------------------------------------------------|------------------------------------------------|---------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------|------------------------------------------------------------|----------------------------------------------------------------|-------------------------------------------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------------------|-----------------------------------------------|-----------------------------------------------------------|------------------------------------------------------|-------------------------------------------------|------------------------------------------------|---------------------------------|---------------------------------|
| positive regulation of cell differentiation            | neuron projection development                              | positive regulation of cellular component organization | regulation of nervous system development         | regulation of gene expression                    | striated muscle tissue development              | gliogenesis                                    |                                                   | transmembrane receptor protein tyrosine kinase signaling pathway |                                                                  | cellular response to growth factor stimulus                        |                                                            |                                                                | positive regulation of cell communication                         |                                                                 | epithelial cell migration                                                    | endocytosis                                   | peptide hormone secretion                                 | histamine secretion                                  | smooth muscle contraction                       |                                                |                                 |                                 |
|                                                        | positive regulation of cell death                          | regulation of protein metabolic process                | transcription, DNA-templated                     | regulation of cellular protein metabolic process | RNA biosynthetic process                        | lacrimal gland development                     | oligodendrocyte differentiation                   | regulation of RNA metabolic process                              | positive regulation of signal transduction                       | cyclic-nucleotide-mediated signaling                               | anterograde trans-synaptic signaling                       | negative regulation of cell communication                      | regulation of blood circulation                                   | regulation of transmembrane transport                           | organic acid transmembrane transport                                         | anion transport                               | relaxation of cardiac muscle                              |                                                      |                                                 |                                                |                                 |                                 |
|                                                        |                                                            |                                                        |                                                  |                                                  |                                                 |                                                |                                                   |                                                                  |                                                                  |                                                                    |                                                            |                                                                |                                                                   |                                                                 |                                                                              |                                               |                                                           |                                                      |                                                 |                                                |                                 |                                 |
|                                                        |                                                            |                                                        |                                                  |                                                  |                                                 |                                                |                                                   |                                                                  |                                                                  |                                                                    |                                                            |                                                                |                                                                   |                                                                 |                                                                              |                                               |                                                           |                                                      |                                                 |                                                |                                 |                                 |
| positive regulation of macromolecule metabolic process | striated muscle cell differentiation                       | regulation of macromolecule biosynthetic process       | negative regulation of biosynthetic process      | bone mineralization                              | regulation of cardiocyte differentiation        | lamellipodium organization                     | dendritic spine morphogenesis                     | regulation of nucleobase-containing compound metabolic process   | regulation of intracellular signal transduction                  | negative regulation of signal                                      | regulation of Notch signaling                              | ERK1 and ERK2 cascade                                          | regulation of secretion                                           | intracellular transport                                         | regulation of amine transport                                                | azole transport                               | amine transport                                           |                                                      |                                                 |                                                |                                 |                                 |
| regulation of cell morphogenesis                       |                                                            | regulation of osteoblast development                   | neural crest cell development                    | ureter urothelium development                    | odontogenesis of dentin-containing tooth        | positive regulation of developmental growth    | hindlimb morphogenesis                            | regulation of cartilage development                              | transmembrane receptor protein tyrosine kinase signaling pathway |                                                                    |                                                            |                                                                | positive regulation of cellular component movement                | organic anion transport                                         | regulation of neurotransmitter transport                                     | regulation of lipid transport                 | vesicle-mediated transport in synapse                     | L-glutamate transport                                |                                                 |                                                |                                 |                                 |
| positive regulation of cell proliferation              | hemopoiesis                                                | positive regulation of cell differentiation            |                                                  |                                                  |                                                 |                                                |                                                   | Fc receptor mediated stimulatory signaling pathway               | positive regulation of response to external stimulus             | phosphorylation                                                    | phosphorus metabolic process                               | response to corticosteroid                                     | regulation of ion transport                                       | organic acid transport                                          | regulation of systemic arterial blood pressure mediated by a chemical signal | physiological muscle hypertrophy              | monoamine transport                                       | regulation of ion transmembrane transporter activity |                                                 |                                                |                                 |                                 |
|                                                        | female gonad development                                   | death                                                  | brain segmentation                               | epithelial cell proliferation                    | regulation of nitric oxide biosynthetic process | cell apoptotic process                         | kidney epithelium development                     | regulation of organelle organization                             | compartment pattern specification                                | regulation of G-protein coupled receptor protein signaling pathway | response to monosaccharide                                 | positive regulation of immune response                         |                                                                   |                                                                 | regulation of platelet-derived growth factor receptor signaling pathway      | response to amine                             | regulation of establishment of protein localization       | drug transmembrane transport                         | import across plasma membrane                   | ammonium transport                             |                                 |                                 |
| chordate embryonic development                         | negative regulation of cell proliferation                  | regulation of organ morphogenesis                      | dendrite extension                               | negative regulation of cell growth               | cardiac right ventricle morphogenesis           | metanephric glomerulus vasculature development | RNA metabolic process                             | regulation of male gonad development                             | regulation of somitogenesis                                      | phosphatidylinositol-mediated signaling                            | regulation of leukocyte chemotaxis                         | cellular response to peptide                                   | cellular response to histamine                                    | regulation of long-term neuronal synaptic plasticity            | Wnt signaling pathway                                                        | regulation of actin cytoskeleton organization | regulation of supramolecular fiber organization           | positive regulation of hydrolase activity            | positive regulation of transferase activity     | negative regulation of cell-substrate adhesion |                                 |                                 |
| ear development                                        |                                                            | melanocyte differentiation                             | regulation of stem cell proliferation            | regulation of epithelial cell differentiation    | lung epithelial cell differentiation            | negative regulation of bone development        | columnar/cuboidal epithelial cell differentiation | acylglycerol biosynthetic process                                | megakaryocyte development                                        |                                                                    | regulation of macrophage derived foam cell differentiation | cellular response to alcohol                                   | cellular response to ketone                                       | cellular response to brain-derived neurotrophic factor stimulus | response to isoquinoline alkaloid                                            | cytoskeleton organization                     | adherens junction assembly                                | plasma membrane invagination                         | regulation of lipase activity                   | regulation of lipase activity                  | cell-substrate adhesion         |                                 |
|                                                        |                                                            |                                                        |                                                  |                                                  |                                                 |                                                |                                                   |                                                                  |                                                                  |                                                                    | regulation of macrophage derived foam cell differentiation | cellular response to lipid                                     | cellular response to retinoic acid                                | nitric oxide mediated signal transduction                       | regulation of fibroblast growth factor receptor signaling pathway            | response to calcium ion                       | regulation of neurotrophin TRK receptor signaling pathway | protein localization to membrane                     | regulation of extracellular matrix organization | cellular homeostasis                           | cellular cation homeostasis     | intestinal epithelial structure |
| regulation of angiogenesis                             | negative regulation of nitrogen compound metabolic process | pancreatic PP cell fate commitment                     | spinal cord oligodendrocyte cell differentiation | central nervous system neuron differentiation    | myeloid progenitor cell differentiation         | positive regulation of lipid metabolic process | superoxide anion generation                       | adult heart development                                          | pseudopodium organization                                        | cellular response to organic cyclic compound                       | cellular response to retinoic acid                         | cellular response to nitric oxide mediated signal transduction | regulation of fibroblast growth factor receptor signaling pathway | response to calcium ion                                         | regulation of neurotrophin TRK receptor signaling pathway                    | protein localization to membrane              | regulation of extracellular matrix organization           | cellular homeostasis                                 | cellular cation homeostasis                     | intestinal epithelial structure                | cardiac muscle action potential | mast cell mediated immunity     |

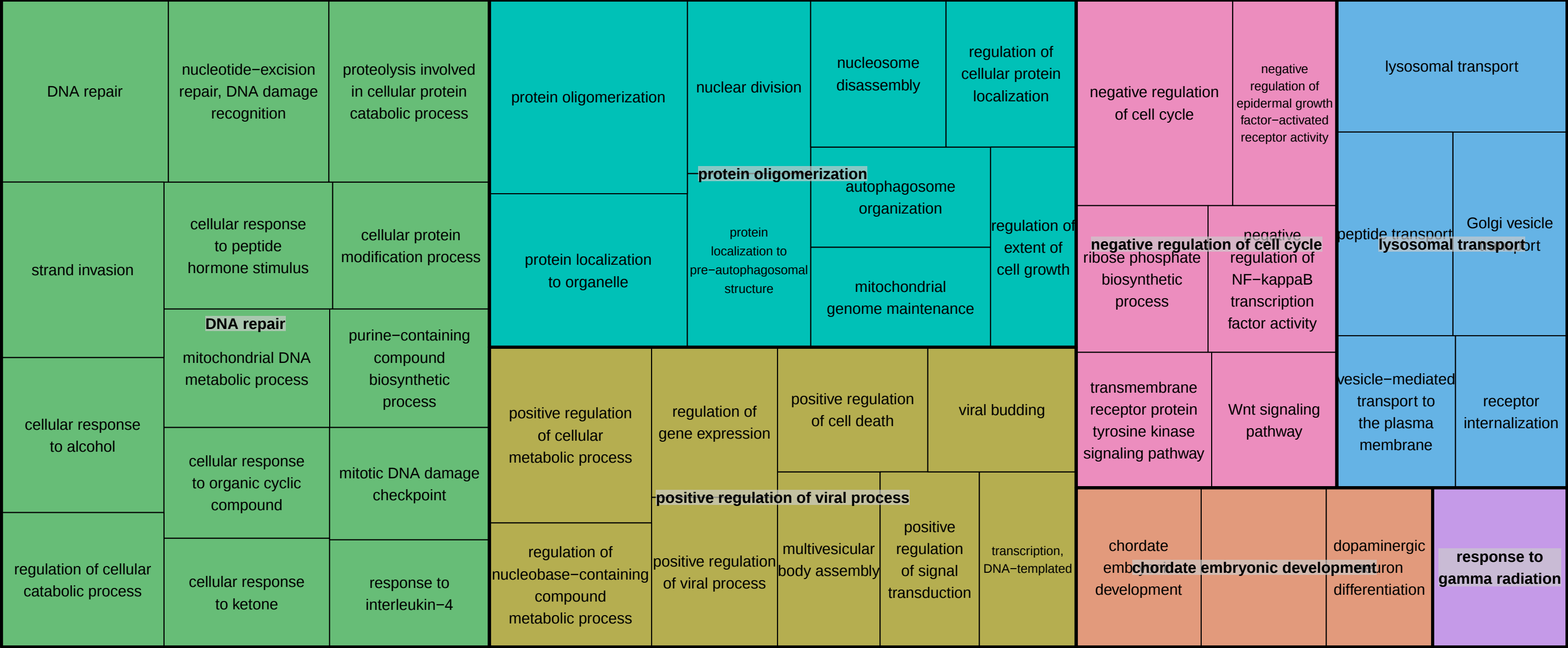
Common Hypovariable Essential GO Annotations



Hypovariable Essential GO Annotations in Breast Tissue



Hypovariable Essential GO Annotations in Cerebellum Tissue



Hypovariable Essential GO Annotations in Frontal Cortex Tissue

|                                                                |                                       |                                                        |                                                 |                                                                           |                                             |                                               |                                                |                                                    |                                                                          |                                            |                                             |                                          |
|----------------------------------------------------------------|---------------------------------------|--------------------------------------------------------|-------------------------------------------------|---------------------------------------------------------------------------|---------------------------------------------|-----------------------------------------------|------------------------------------------------|----------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------|---------------------------------------------|------------------------------------------|
| DNA repair                                                     | RNA metabolic process                 | negative regulation of macromolecule metabolic process | negative regulation of signal transduction      | regulation of cellular protein metabolic process                          | regulation of protein metabolic process     | cellular response to steroid hormone stimulus | DNA biosynthetic process                       | nucleotide–excision repair, DNA damage recognition | protein localization to organelle                                        | mRNA transport                             | lysosomal transport                         |                                          |
| regulation of gene expression                                  |                                       | transcription, DNA–templated                           | regulation of ERBB signaling pathway            | proteolysis involved in cellular protein catabolic process                | progesterone receptor signaling pathway     | regulation of programmed cell death           | death–inducing signaling complex assembly      | nuclear division                                   |                                                                          |                                            |                                             | peptide transport                        |
|                                                                | Wnt signaling pathway                 |                                                        |                                                 | endosome organization                                                     | Ras protein signal transduction             | cellular response to cytokine stimulus        | positive regulation of immune effector process | peptide transport                                  | positive regulation of exosomal secretion                                | nucleobase–containing compound transport   | regulation of cellular protein localization |                                          |
|                                                                |                                       |                                                        |                                                 |                                                                           |                                             |                                               |                                                |                                                    |                                                                          |                                            |                                             | RNA biosynthetic process                 |
| regulation of nucleobase–containing compound metabolic process | regulation of RNA metabolic process   | histone modification                                   | regulation of intracellular signal transduction | protein oligomerization                                                   | cellular response to growth factor stimulus | positive regulation of leukocyte activation   | DNA modification                               | interleukin–1–mediated signaling pathway           | transmembrane receptor protein serine/threonine kinase signaling pathway | regulation of type I interferon production | spleen development                          | response to UV                           |
|                                                                |                                       |                                                        |                                                 | innate immune response activating cell surface receptor signaling pathway | cellular response to ketone                 | response to interleukin–15                    | positive regulation of hemopoiesis             | stress–activated MAPK cascade                      | regulation of platelet–derived growth factor receptor signaling pathway  |                                            |                                             |                                          |
| positive regulation of macromolecule metabolic process         | cellular protein modification process | positive regulation of signal transduction             | positive regulation of cell communication       |                                                                           |                                             |                                               |                                                |                                                    |                                                                          | multivesicular body assembly               | interleukin–15–mediated signaling pathway   | regulation of cellular catabolic process |
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