

Summary of the Identified Clusters

Cluster 0 — Aerobic Energy Metabolism and Electron Transport Chain

This cluster is strongly characterized by oxidative phosphorylation, aerobic respiration, and electron transport. The predominant molecular functions involve electron transfer, proton transport, and cytochrome activity. Localization is clearly mitochondrial, with high representation of the inner membrane and complex I. Overall, this cluster includes key genes of cellular oxidative metabolism.

Cluster 1 — Enhanced Mitochondrial Respiration and Complex I

This cluster is tightly linked to the transfer of electrons from NADH to ubiquinone. Molecular functions are dominated by NADH dehydrogenase activity, and cellular components belong almost exclusively to respiratory chain complex I. It represents the NADH-dependent component of mitochondrial respiration with strong specificity.

Cluster 2 — Epidermal Differentiation and Epithelial Cytoskeleton

The main processes include keratinocyte proliferation and differentiation, skin development, and activation of the JAK-STAT pathway. Molecular functions are typical of structural proteins in the epidermis and cytoskeleton. Localization includes intermediate filaments, cell junctions, and the cornified envelope. This cluster reflects skin biology and structural features of epithelial tissues.

Cluster 3 — Protein Translation and Ribosome Biogenesis

The cluster focuses on translation processes and ribosome assembly. Molecular functions and cellular components clearly identify ribosomal proteins and cytoplasmic ribonucleoprotein complexes. It is highly coherent with protein synthesis and ribosomal subunit biogenesis.

Cluster 4 – Cell Motility, Cilia, and Dynein Complexes

This cluster includes microtubule-dependent processes, particularly ciliary movement, axoneme organization, and formation of motile cilia. Molecular functions involve motor proteins such as dyneins and microtubule-associated ATPases. Cellular components include the dynein complex, axoneme, and other ciliary structures.

It represents the ciliary and microtubule-based motility machinery.

Cluster 5 – Transcription Regulation and Nuclear Factors

Processes are centered on positive and negative regulation of transcription mediated by RNA polymerase II. Molecular functions highlight DNA binding, regulatory activity, and promoter recognition. Localization is nuclear, involving chromatin and transcriptional regulatory complexes.

This cluster represents nuclear transcriptional regulators.

Cluster 6 – Ion Transport and Channel Activity

Dominated by ion transport, especially cations. Molecular functions include ion channel and transmembrane transporter activity. Localization shows ion channel complexes and the plasma membrane.

This cluster is coherent with cellular electrical physiology and ion transport systems.

Cluster 7 – Extracellular Matrix and Collagen Organization

Biological processes focus on extracellular matrix formation and collagen fibril organization. Molecular functions represent structural ECM components and collagen molecules. Localization is consistent with ECM sites and the endoplasmic reticulum, where ECM proteins are synthesized.

A typical connective tissue and ECM-related cluster.

Cluster 8 — RNA Processing and Splicing

Processes are strongly related to RNA processing, splicing, and mRNA maturation. Molecular functions include RNA binding and ribonuclease activity. Localization corresponds to ribonucleoprotein complexes and the spliceosome. This cluster represents post-transcriptional RNA regulation.

Cluster 9 — DNA Repair and Genome Stability

Processes include DNA repair, damage response, recombination, and telomere maintenance. Molecular functions involve DNA binding and ATPase activity associated with DNA remodeling. Localization is nuclear, particularly in chromosomal and telomeric regions.

This cluster is clearly associated with DNA damage response and genome stability.

Cluster 10 — Ubiquitination and Protein Quality Control

Processes involve ubiquitin-dependent protein modification and proteasomal degradation. Molecular functions show ubiquitin-ligase activity and protein transfer enzymes. Cellular components correspond to ubiquitination complexes and proteasomes.

A typical cluster of the ubiquitin–proteasome protein degradation system.

Cluster 11 — Solute and Anion Transport at the Apical Membrane

Processes center on transport of organic and inorganic anions and transmembrane solute movement. Molecular functions are characteristic of sodium/solute symporters. Localization is at the apical plasma membrane of epithelial cells. A cluster consistent with epithelial solute transport.

Cluster 12 — Weak Cell Signaling and Low-Specificity Receptors

A weak and poorly cohesive cluster. Terms point to membrane receptors and kinases, but with low scores and heterogeneous localization. Signaling processes are

present but not dominant.

A heterogeneous cluster without a clear biological theme.

Cluster 13 — Antigen Presentation and MHC Pathways

Highly coherent with antigen presentation and MHC class I/II pathways. Molecular functions include peptide binding and peptidase activities. Cellular components comprise endosomes, lysosomes, ER-Golgi compartments, and trafficking vesicles. A representative cluster of antigen-presenting cells (APCs).

Cluster 14 — Cytokine Signaling and Immune Response

Processes reflect cytokine-mediated signaling and cellular response to immune stimuli. Molecular functions involve cytokine receptors and transmembrane signaling. Localization is at the cell surface and membrane signaling complexes. A cluster typical of inflammatory signal transduction.

Cluster 15 — Glycoprotein and Proteoglycan Biosynthesis (Golgi)

Processes involve synthesis and metabolism of glycoproteins and proteoglycans. Molecular functions are dominated by glycosyltransferase activity. Cellular components show strong localization in the Golgi apparatus. A cluster consistent with protein glycosylation pathways.

Cluster 16 — Complex Carbohydrate Metabolism and Lysosomal Degradation

Processes relate to metabolism of carbohydrates, glycolipids, and glycosphingolipids. Molecular functions are typical of glycosidic hydrolases. Localization in lysosomes and degradative compartments confirms the catabolic role.

A cluster representing lysosomal degradation of complex biomolecules.

Cluster 17 — Actin Cytoskeleton and Cell Motility

Processes concern actin organization, contraction, and cell motility. Molecular functions include actin binding and regulation of contractile fibers. Cellular components include the actin cytoskeleton and sarcomeres.

A cluster associated with cellular movement and actin-myosin structures.

Cluster 18 — Amino Acid and Organic Acid Metabolism (Mitochondrial)

Processes involve metabolism of amino acids, organic acids, and TCA cycle intermediates. Molecular functions are characteristic of oxidoreductases and metabolic enzymes. Localization is mainly mitochondrial.

A cluster consistent with mitochondrial energy metabolism.

Cluster 19 — Lipid Metabolism and Endoplasmic Reticulum Enzymatic Pathways

Processes focus on lipid and phospholipid biosynthesis. Molecular functions involve oxidoreductase, monooxygenase (cytochrome P450), and transferase activities. Cellular components localize these enzymes in the endoplasmic reticulum.

A cluster typical of ER-based lipid synthesis.

Cluster 20 — Extracellular Matrix, Cell Adhesion, and Tissue Remodeling

Processes include ECM organization, cell adhesion, and tissue development. Molecular functions include ECM structural components and metalloproteases. Localization is extracellular and within the basement membrane.

A cluster consistent with tissue remodeling and ECM dynamics.

Cluster 21 — Immune Response and Inflammatory Signaling

Processes span innate and adaptive immune responses. Molecular functions involve membrane and cytokine receptors. Localization is at the cell surface and

extracellular vesicles.

A cluster representing immune activation and regulation.

Cluster 22 — Microtubule Cytoskeleton and Cell Division

Processes are associated with microtubule-based functions, cytoskeleton organization, and the mitotic cycle. Molecular functions indicate motor protein activity (kinesins, dyneins). Localization includes the microtubule cytoskeleton, centrosomes, and centrioles.

A cluster related to microtubule dynamics and cell division.

Cluster 23 — Vesicle Trafficking and Endomembrane System

Processes include intracellular transport, endocytosis, exocytosis, and vesicle trafficking. Molecular functions involve SNARE binding and transport regulators. Localization is in endosomes, Golgi, and transport vesicles.

A cluster that represents the endomembrane trafficking system.

Cluster 24 — Signal Transduction Mediated by Small GTPases

Processes involve intracellular signaling mediated by small GTPases (Rho, Ras, Rab). Molecular functions indicate GTPase regulators (GEFs, GAPs, GDIs). Localization is cytoplasmic and endomembranous, though less defined.

A cluster typical of regulators of intracellular signaling and vesicle trafficking.