Task 3. GO Enrichment For DMD Genes in Homo Sapiens

Github link: https://github.com/Allen-ZKW/NLP_HZAU/tree/Task3

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Abstract

Gene ontology database is a set of concepts. In this task, we want to do GO enrichment for genes which is concerning to DMD in Homo sapiens in order to find out concepts that have close links to these genes

Principle

$$Hypergeometric\ Distribution$$
$$X \sim H(n, M, N)$$
$$This\ Distribution\ describes\ the\ number\ of\ times\ that\ k\ sepcial\ objects\ are\ successfully\ extracted\ from\ a\ finite\ number\ of\ N\ objects(including\ M\ special\ objects)$$
$$P(x = k) = \frac{C_M^k \cdot C_{N-M}^{n-k}}{C_N^n}$$
$$P\_value = \sum_k^M P(k)$$
$$When\ P\_value\ is\ very\ small,\ this\ will\ reflect\ significant\ difference\ between\ our\ samples\ and\ random\ samples$$

Measure

1. Download Gene Symbols

Download Gene Symbols about DMD in Homo sapiens from: https://www.ncbi.nlm.nih.gov/gene

Clean the data of search information file by Excel to only save gene symbols

2. Download and import Essential Packages

```
install.packages('devtools', repos =
'https://mirrors.tuna.tsinghua.edu.cn/CRAN')
install.packages('BiocManager', repos =
'https://mirrors.tuna.tsinghua.edu.cn/CRAN')
install.packages("cli", repos = 'https://mirrors.tuna.tsinghua.edu.cn/CRAN')
library('devtools')
BiocManager::install(version = "3.12")
```

```
Needed=c("bit", "formatR", "hms", "triebeard", "tweenr", "polyclip",
"RcppEigen", "RcppArmadillo", "zlibbioc", "bit64", "blob", "plogr", "lambda.r",
"futile.options", "progress", "urltools", "gridGraphics", "ggforce", "ggrepel",
"viridis", "tidygraph", "graphlayouts", "bitops", "XVector", "IRanges",
"RSQLite", "futile.logger", "snow", "data.table", "gridExtra", "fastmatch",
"cowplot", "europepmc", "ggplotify", "ggraph", "ggridges", "igraph", "dplyr",
"tidyselect", "RCurl", "Biostrings", "AnnotationDbi", "BiocParallel", "DO.db",
"fgsea", "GOSemSim", "qvalue", "S4Vectors", "BiocGenerics", "graph", "Biobase",
"GO.db", "SparseM", "matrixStats", "DBI", "enrichplot", "rvcheck", "tidyr",
"org.Hs.eg.db", "KEGGgraph", "XML", "Rgraphviz", "png", "KEGGREST")
B_I <- c("DOSE","topGO","clusterProfiler","pathview")
install.packages(Needed, repos = 'https://mirrors.tuna.tsinghua.edu.cn/CRAN')
BiocManager::install(B_I)
library(DOSE)
library(org.Hs.eg.db)
library(topGO)
library(clusterProfiler)
library(pathview)
```

3. GO Enrichment

1) Read Data from CSV File

```
MyGeneSet <- read.table('D:/junior_n/NLP/task_3/data/gene_result.csv')
MyGeneSet <- as.character(MyGeneSet$V1)
```

2) Transform from SYMBOL to ENSEMBL, ENTREZID and GO

```
MyGeneIDSet <- bitr(MyGeneSet,
                    fromType="SYMBOL",
                    toType=c("ENSEMBL","ENTREZID","GO"),
                    OrgDb="org.Hs.eg.db")
```

3) Use DOSE Package to Get Background Genes for GO Enrichment

```
data(geneList, package="DOSE")
```

4) GO Enrichment in All GO Domains

```
ego_ALL <- enrichGO(gene = MyGeneIDSet$ENTREZID,
                    universe = names(geneList),
                    OrgDb = org.Hs.eg.db,
                    ont = "ALL",
                    pAdjustMethod = "BH",
                    pvalueCutoff = 1,
                    qvalueCutoff = 1,
                    readable = TRUE)
```

5) GO Enrichment in Molecular Function, Cellular Component and Biological Process

```
ego_MF <- enrichGO(gene = MyGeneIDSet$ENTREZID,
                   universe = names(geneList),
                   OrgDb = org.Hs.eg.db,
                   ont = "MF",
                   pAdjustMethod = "BH",
                   pvalueCutoff = 1,
                   qvalueCutoff = 1,
                   readable = TRUE)

ego_CC <- enrichGO(gene = MyGeneIDSet$ENTREZID,
                   universe = names(geneList),
                   OrgDb = org.Hs.eg.db,
                   ont = "CC",
                   pAdjustMethod = "BH",
                   pvalueCutoff = 1,
                   qvalueCutoff = 1,
                   readable = TRUE)

ego_BP <- enrichGO(gene = MyGeneIDSet$ENTREZID,
                   universe = names(geneList),
                   OrgDb = org.Hs.eg.db,
                   ont = "BP",
                   pAdjustMethod = "BH",
                   pvalueCutoff = 1,
                   qvalueCutoff = 1,
                   readable = TRUE)
```

4. Visualization

1) Draw Dotplot for each GO Enrichment result

```
png("D:/junior_n/NLP/task_3/result/MF_DOT.png",units="in", width=10,
height=10,res=500)
dotplot(ego_MF,title="EnrichmentGO_MF_dot")
dev.off()
png("D:/junior_n/NLP/task_3/result/CC_DOT.png",units="in", width=10,
height=10,res=500)
dotplot(ego_CC,title="EnrichmentGO_CC_dot")
dev.off()
png("D:/junior_n/NLP/task_3/result/BP_DOT.png",units="in", width=10,
height=10,res=500)
dotplot(ego_BP,title="EnrichmentGO_BP_dot")
dev.off()
```

2) Draw barplot for each GO Enrichment result

```
png("D:/junior_n/NLP/task_3/result/MF_BAR.png",units="in", width=10,
height=10,res=500)
barplot(ego_MF, showCategory=20,title="EnrichmentGO_MF_bar")
dev.off()
png("D:/junior_n/NLP/task_3/result/CC_BAR.png",units="in", width=10,
height=10,res=500)
barplot(ego_CC, showCategory=20,title="EnrichmentGO_CC_bar")
dev.off()
png("D:/junior_n/NLP/task_3/result/BP_BAR.png",units="in", width=10,
height=10,res=500)
barplot(ego_BP, showCategory=20,title="EnrichmentGO_BP_bar")
dev.off()
```

3) Draw GO Graph for each GO Enrichment result

```
png("D:/junior_n/NLP/task_3/result/MF_GG.png",units="in", width=5,
height=5,res=500)
plotGOgraph(ego_MF,firstSigNodes = 10, useInfo = "all", sigForAll =
TRUE,useFullNames = TRUE)
dev.off()
png("D:/junior_n/NLP/task_3/result/CC_GG.png",units="in", width=5,
height=5,res=500)
plotGOgraph(ego_CC,firstSigNodes = 10, useInfo = "all", sigForAll =
TRUE,useFullNames = TRUE)
dev.off()
png("D:/junior_n/NLP/task_3/result/BP_GG.png",units="in", width=5,
height=5,res=700)
plotGOgraph(ego_BP,firstSigNodes = 10, useInfo = "all", sigForAll =
TRUE,useFullNames = TRUE)
dev.off()
```

Result

1. Related GOs' Name and Definition

1) Molecular Function

GO:0003779

actin binding

Interacting selectively and non-covalently with monomeric or multimeric forms of actin, including actin filaments.

GO:0030165

PDZ domain binding

Interacting selectively and non-covalently with a PDZ domain of a protein, a domain found in diverse signaling proteins.

GO:0002020

protease binding

Interacting selectively and non-covalently with any protease or peptidase.

GO:0005178

integrin binding

Interacting selectively and non-covalently with an integrin

GO:0005125

cytokine activity

The activity of a soluble extracellular gene product that interacts with a receptor to effect a change in the activity of the receptor to control the survival, growth, differentiation and effector function of tissues and cells.

GO:0008307

structural constituent of muscle

The action of a molecule that contributes to the structural integrity of a muscle fiber.

GO:0017166

vinculin binding

Interacting selectively and non-covalently with vinculin, a protein found in muscle, fibroblasts, and epithelial cells that binds actin and appears to mediate attachment of actin filaments to integral proteins of the plasma membrane.

GO:0004197

cysteine-type endopeptidase activity

Catalysis of the hydrolysis of internal, alpha-peptide bonds in a polypeptide chain by a mechanism in which the sulfhydryl group of a cysteine residue at the active center acts as a nucleophile.

GO:0097718

disordered domain specific binding

Interacting selectively and non-covalently with a disordered domain of a protein.

GO:0042805

actinin binding

Interacting selectively and non-covalently with actinin, any member of a family of proteins that crosslink F-actin.

2) Cellular Component

GO:0098797

plasma membrane protein complex

Any protein complex that is part of the plasma membrane.

GO:0042383

sarcolemma

The outer membrane of a muscle cell, consisting of the plasma membrane, a covering basement membrane (about 100 nm thick and sometimes common to more than one fiber), and the associated loose network of collagen fibers.

GO:0062023

collagen-containing extracellular matrix

An extracellular matrix consisting mainly of proteins (especially collagen) and glycosaminoglycans (mostly as proteoglycans) that provides not only essential physical scaffolding for the cellular constituents but can also initiate crucial biochemical and biomechanical cues required for tissue morphogenesis, differentiation and homeostasis. The components are secreted by cells in the vicinity and form a sheet underlying or overlying cells such as endothelial and epithelial cells.

GO:0031012

extracellular matrix

A structure lying external to one or more cells, which provides structural support, biochemical or biomechanical cues for cells or tissues.

GO:0030055

cell-substrate junction

A cell junction that forms a connection between a cell and the extracellular matrix.

GO:0016010

dystrophin-associated glycoprotein complex

A multiprotein complex that forms a strong mechanical link between the cytoskeleton and extracellular matrix; typical of, but not confined to, muscle cells. The complex is composed of transmembrane, cytoplasmic, and extracellular proteins, including dystrophin, sarcoglycans, dystroglycan, dystrobrevins, syntrophins, sarcospan, caveolin-3, and NO synthase.

GO:0090665

glycoprotein complex

A protein complex containing at least one glycosylated protein, may be held together by both covalent and noncovalent bonds.

GO:0030016

myofibril

The contractile element of skeletal and cardiac muscle; a long, highly organized bundle of actin, myosin, and other proteins that contracts by a sliding filament mechanism.

GO:0043292

contractile fiber

Fibers, composed of actin, myosin, and associated proteins, found in cells of smooth or striated muscle.

GO:0005796

Golgi lumen

The volume enclosed by the membranes of any cisterna or subcompartment of the Golgi apparatus, including the cis- and trans-Golgi networks.

3) Biological Process

GO:0003012

muscle system process

A organ system process carried out at the level of a muscle. Muscle tissue is composed of contractile cells or fibers.

GO:0006936

muscle contraction

A process in which force is generated within muscle tissue, resulting in a change in muscle geometry. Force generation involves a chemo-mechanical energy conversion step that is carried out by the actin/myosin complex activity, which generates force through ATP hydrolysis.

GO:0007517

muscle organ development

The process whose specific outcome is the progression of the muscle over time, from its formation to the mature structure. The muscle is an organ consisting of a tissue made up of various elongated cells that are specialized to contract and thus to produce movement and mechanical work.

GO:0030198

extracellular matrix organization

A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of an extracellular matrix.

GO:0043062

extracellular structure organization

A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of structures in the space external to the outermost structure of a cell. For cells without external protective or external encapsulating structures this refers to space outside of the plasma membrane, and also covers the host cell environment outside an intracellular parasit.

GO:0060249

anatomical structure homeostasis

A homeostatic process involved in the maintenance of an internal steady state within a defined anatomical structure of an organism, including control of cellular proliferation and death and control of metabolic function. An anatomical structure is any biological entity that occupies space and is distinguished from its surroundings. Anatomical structures can be macroscopic such as a carpel, or microscopic such as an acrosome.

GO:0050900

leukocyte migration

The movement of a leukocyte within or between different tissues and organs of the body.

GO:0048771

The reorganization or renovation of existing tissues. This process can either change the characteristics of a tissue such as in blood vessel remodeling, or result in the dynamic equilibrium of a tissue such as in bone remodeling.

GO:1904645

response to amyloid-beta

Any process that results in a change in state or activity of a cell or an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a amyloid-beta stimulus.

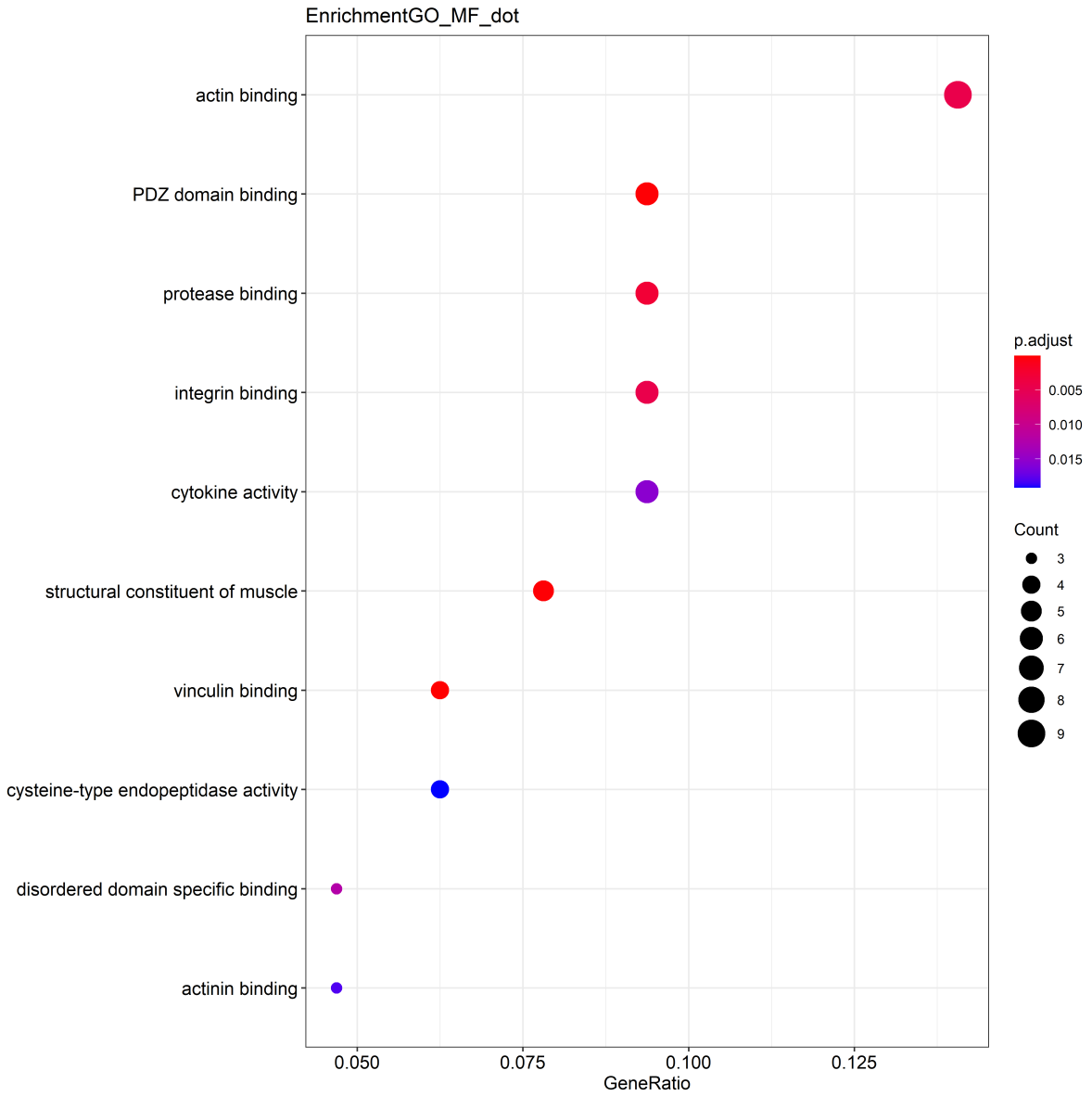
GO:0048641

regulation of skeletal muscle tissue development

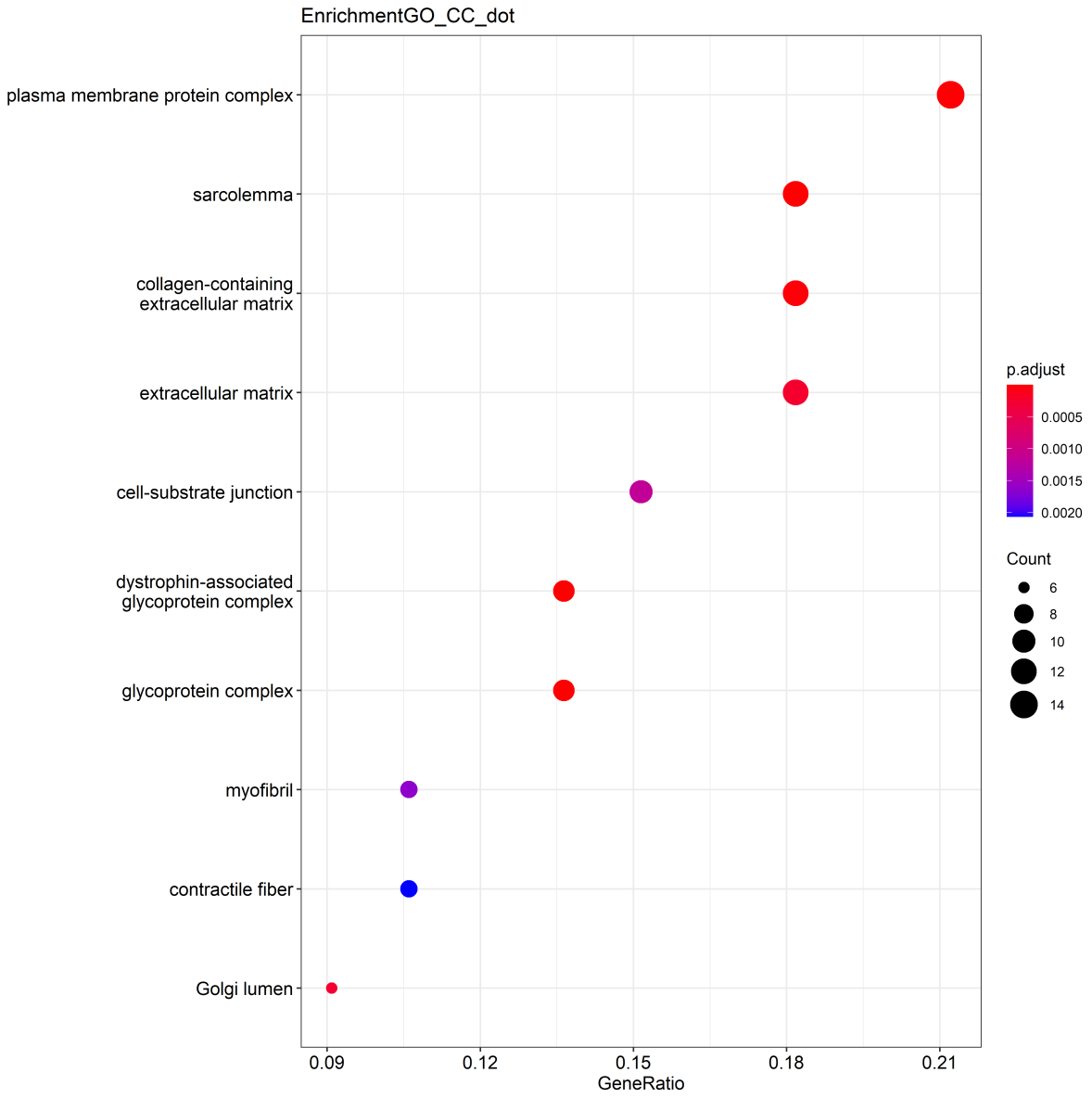
Any process that modulates the frequency, rate or extent of skeletal muscle tissue development.

2. Visualization Result

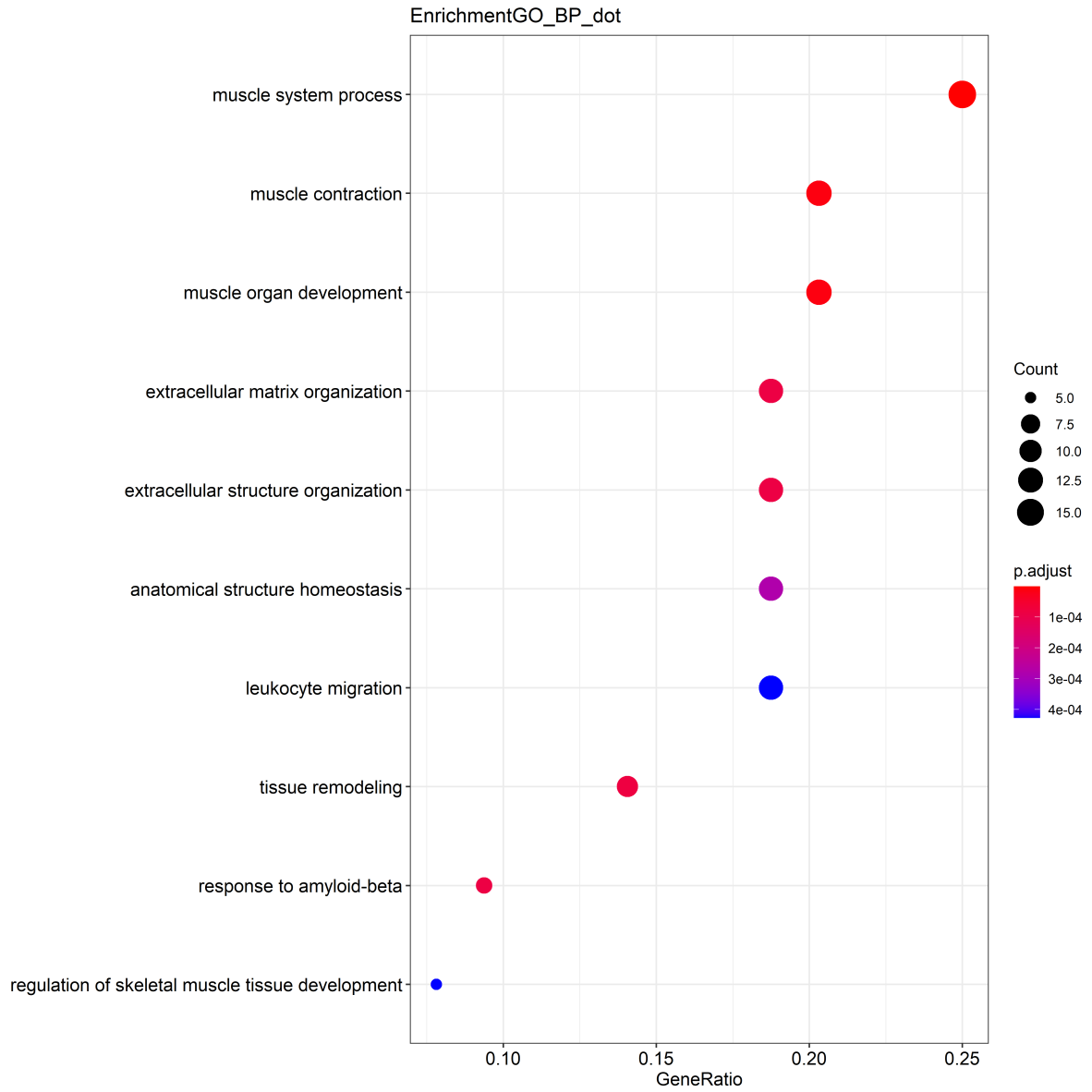
1) GO Enrichment_MF Dotplot



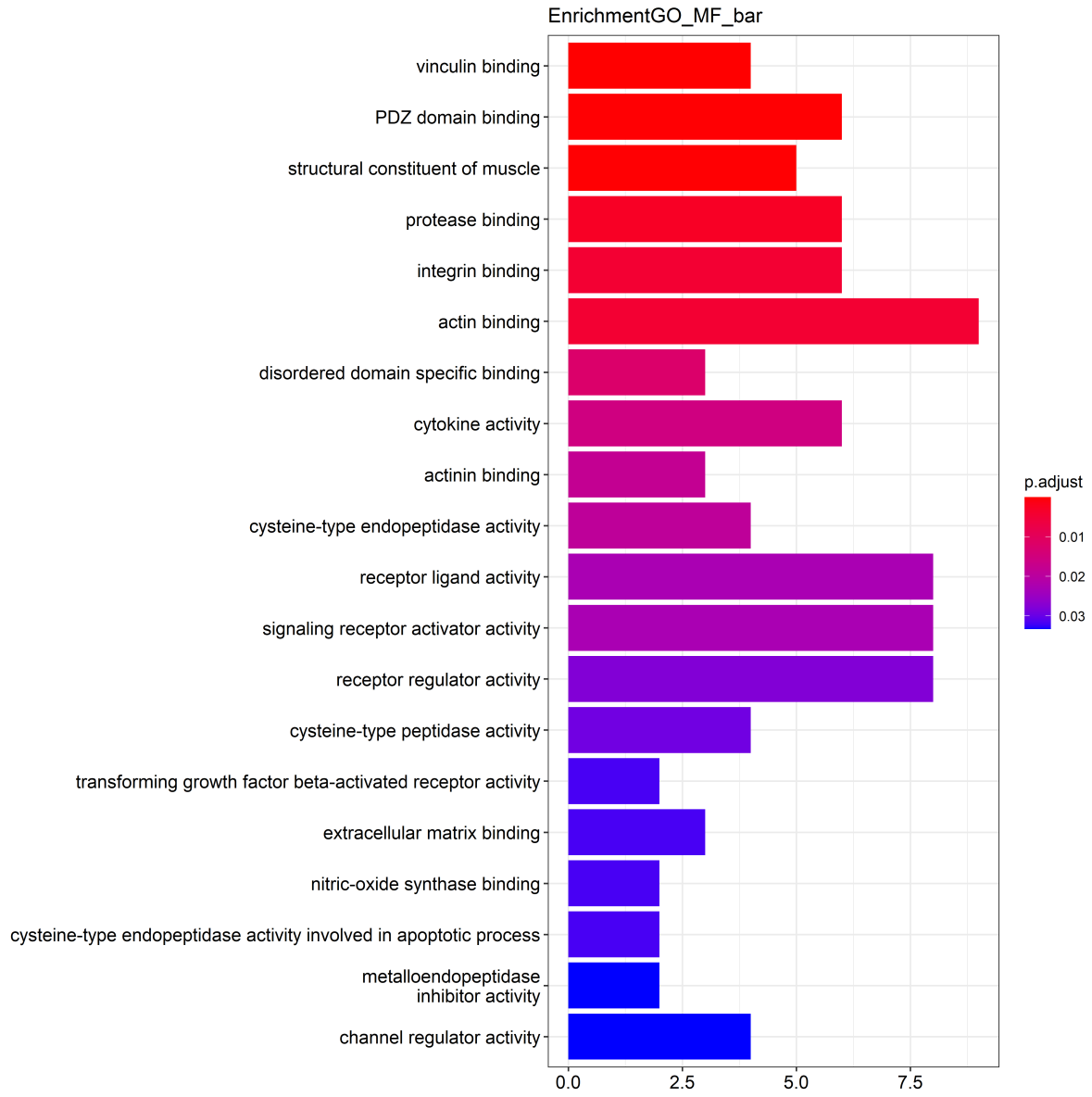
2) GO Enrichment_CC Dotplot



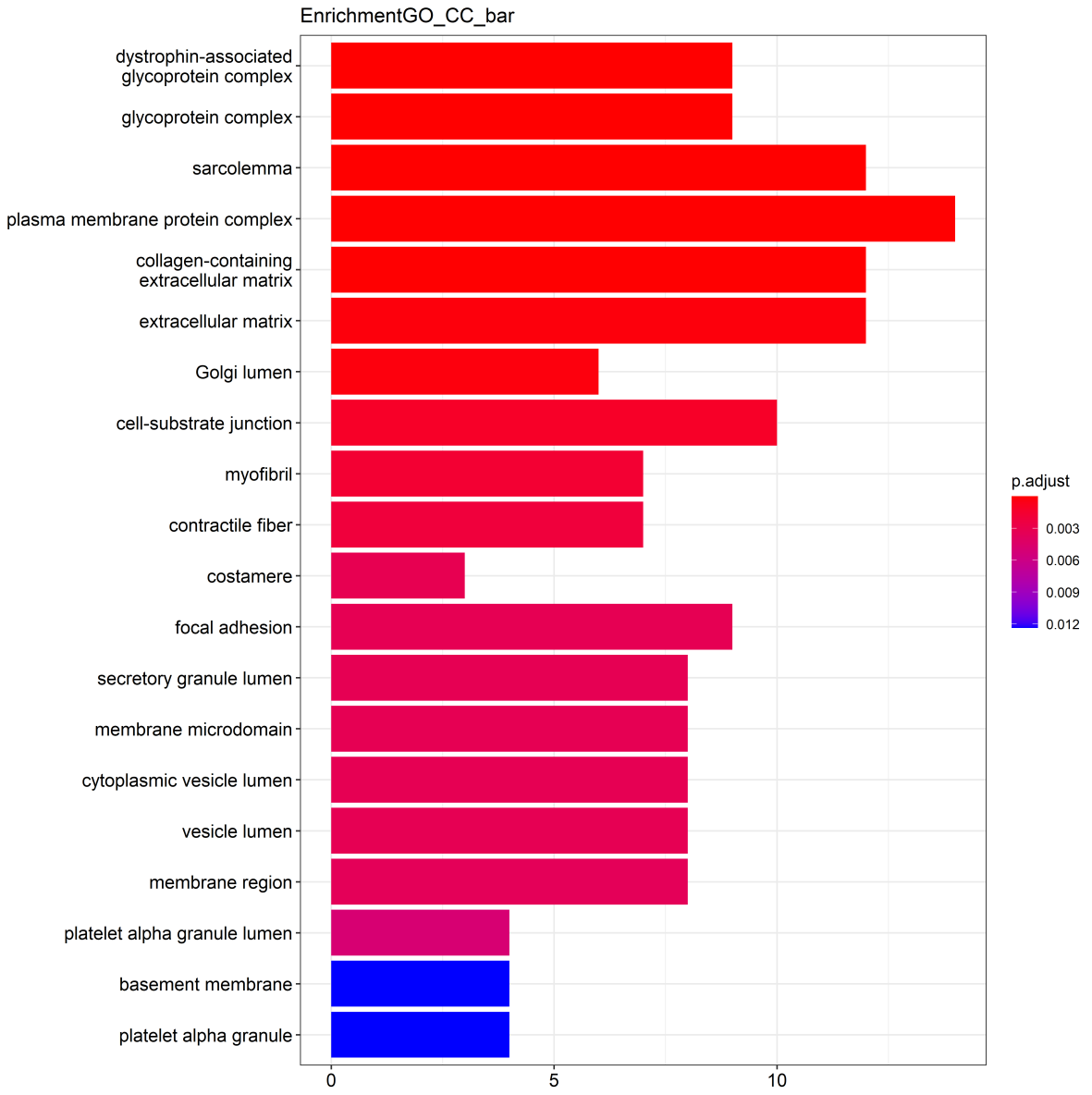
3) GO Enrichment_BP Dotplot



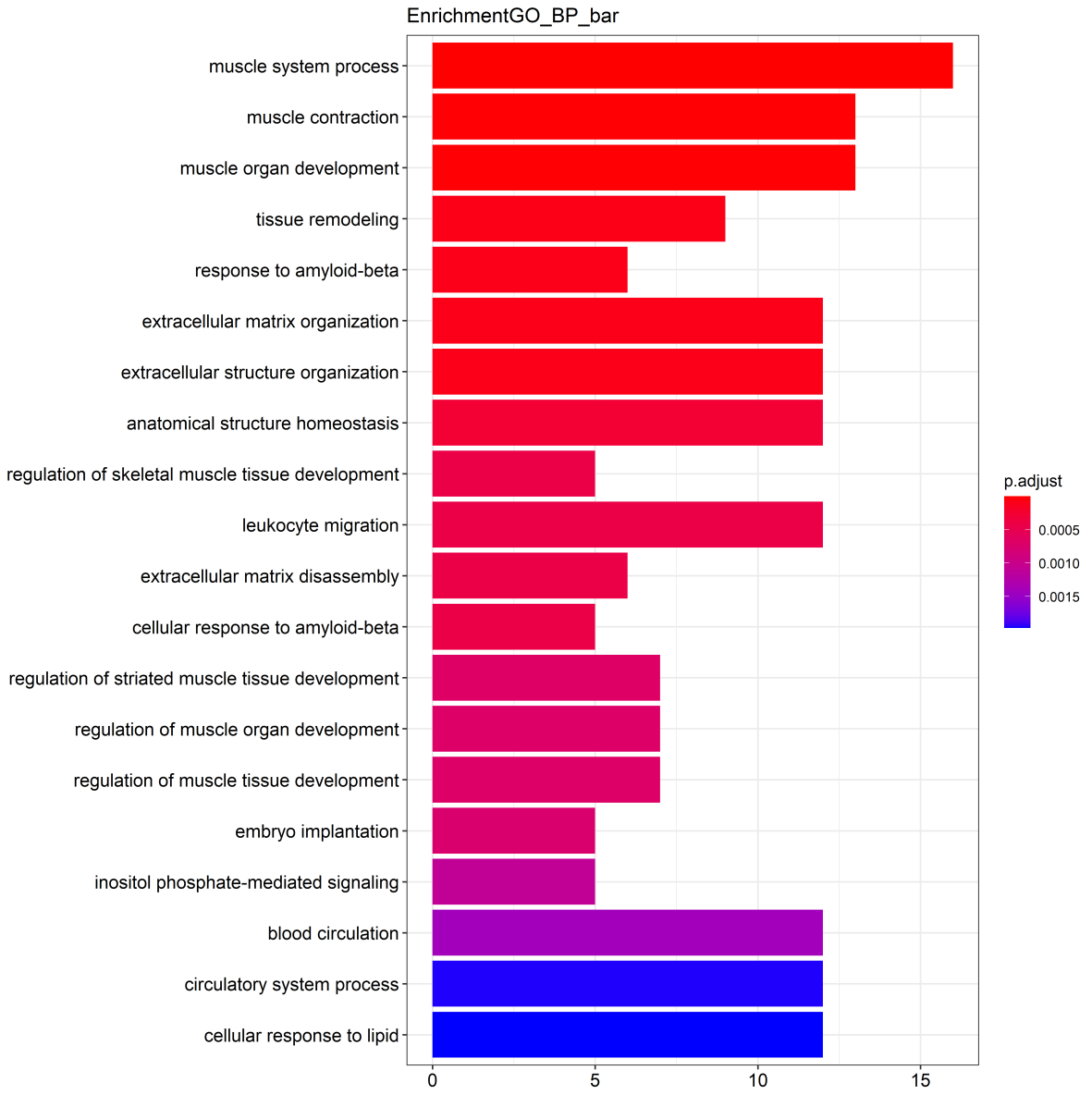
4) GO Enrichment_MF Barplot



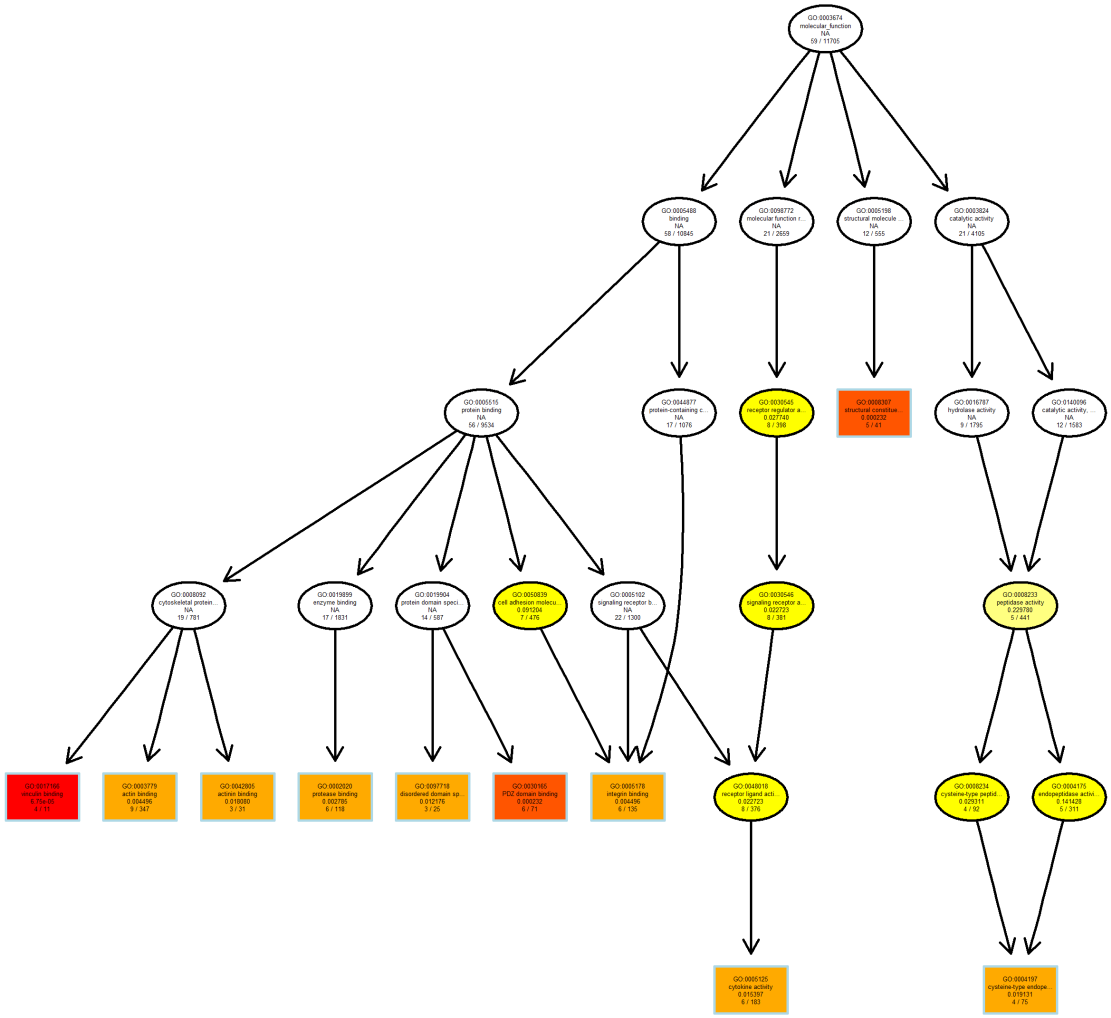
5) GO Enrichment_CC Barplot



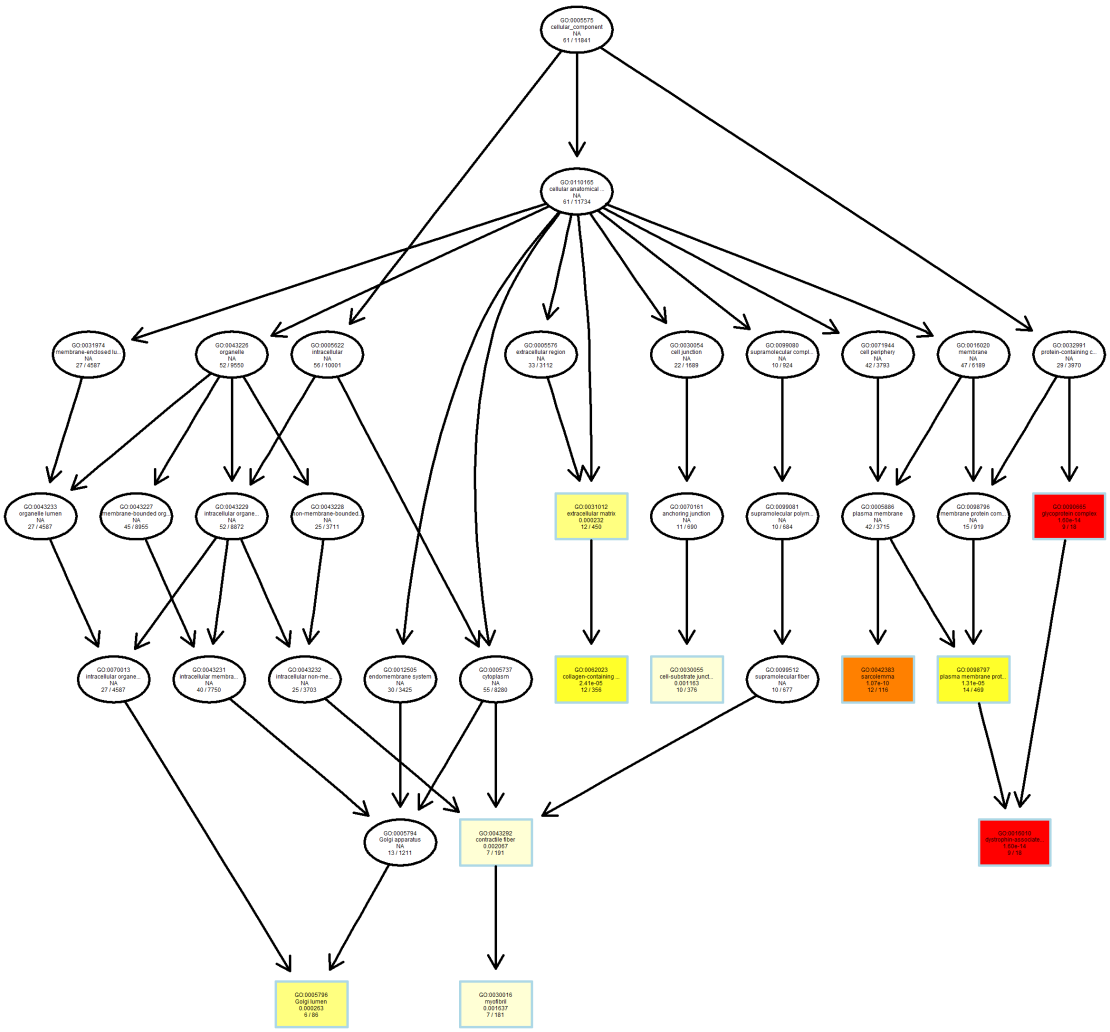
6) GO Enrichment_BP Barplot



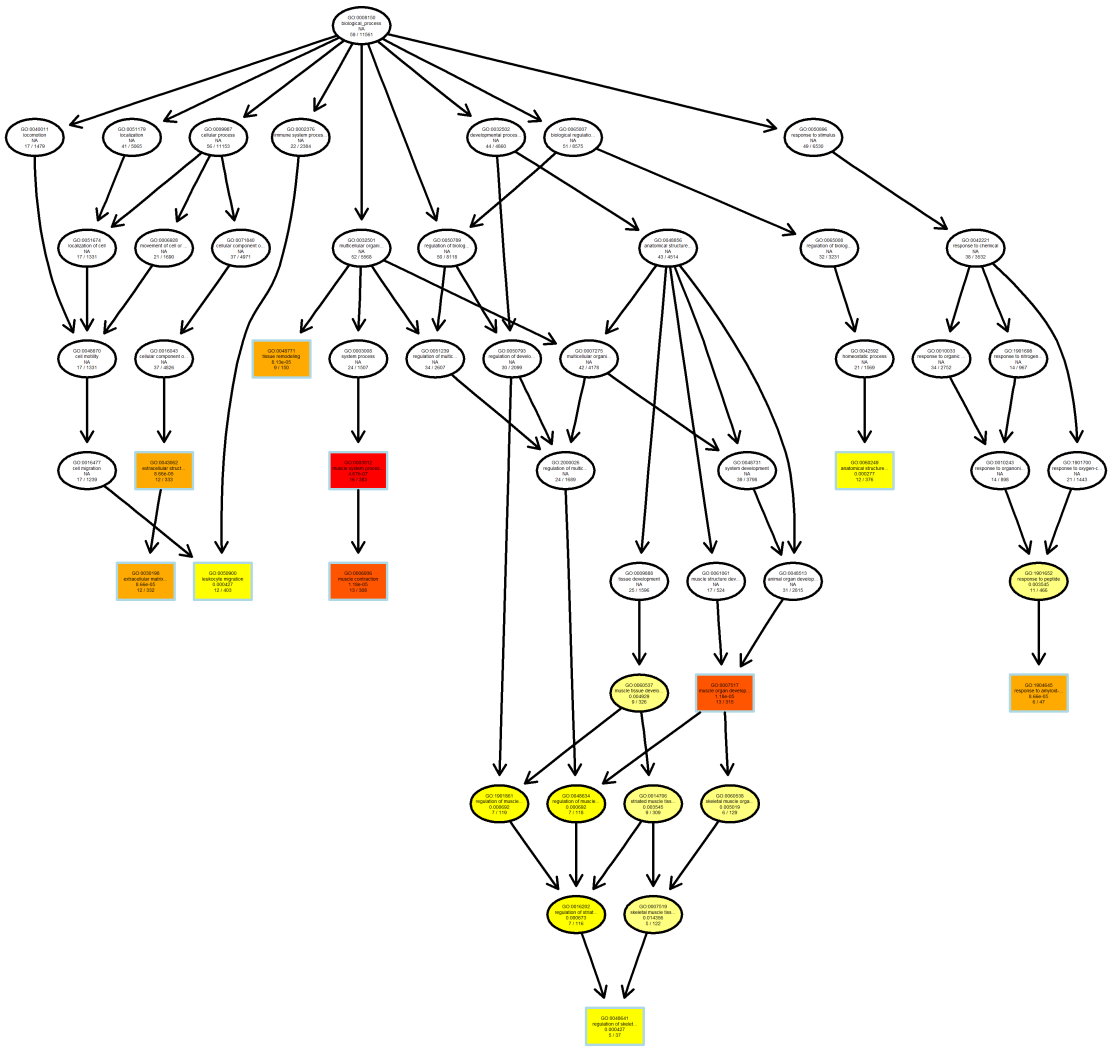
7) GO Enrichment_MF GO graph



8) GO Enrichment_CC GO graph



9) GO Enrichment_BP GO graph



Discussion

By GO enrichment, we gain 30 conceptions from three different gradations in Gene Ontology Database which is closely rated to disease called DMD in Homo sapiens. Searching these results in QuickGO, we get name and definition for each GO terms.

Duchenne Muscular Dystrophy is a muscle disease characterized by body's in ability to form dystrophin protein. This disease has symptoms such as progressive muscle weakness, difficulty walking, enlarged calves, failure to develop motor skills.

In Molecular Function enrichment, the result remarkably gather in two aspects: protein binding and protein activity. Depending on this, DMD may mainly cased by some peptide chains' structures changing which cause these proteins lose related binding with other proteins (or some domains) or factors. Also, these changes also straightly case some proteins inactivation. In the GO graph of Molecular Function, we could discover that these two aspects is mainly separate from each other, however, GO:0005125 and GO:0005178 both have the same parent node: GO:0005102, we believe this reflect the the abnormal phenomena in binding signaling receptor and will infect cells' cytokine activity and interacting selectively and non-covalently with integrin in some degree.

In Cellular Component enrichment, result in this aspect mainly concerns system of intracellular membranes, cells interacting with extracellular components and some glycoprotein complex. The GO graph of cellular component shows that because of abnormal function of Golgi apparatus and Endoplasmic reticulum, glycoprotein complex cannot produce or have the same function as in the healthy body. As is know to all, adhesion and communication is mainly undertake by glycoprotein complex, so the abnormal interaction is closely related to glycoprotein complex.

In Biological Process enrichment, just like the symptoms of this disease, result of this part is mainly about muscle movement and muscle growth. Not only muscle movement and muscle growth itself, but their regulation mechanism also exist in our result. Additionally, GO graph about biological process is the most time-consuming part in my script in the reason of complex relationship and infections between growth, movement and regulation.

Taking all of these into consideration, we infer that: