**The impact of aging specific differentially expressed genes on immuno-pathological regulations**

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ABSTRACT

Aging is defined as an increase in failure (mortality) rate that is irreversible and in biological mechanisms leading to progressive functional decline and increased risk for disease and death. We characterized aging at the gene expression level using GSE32719 data set publicly available at gene expression omnibus (GEO) and ArrayExpress. Using Biobase, GEOquery, gplots packages 96 genes that shows up and down regulation (p < 0.05 and fold change < 0.05). We then investigate gene ontology (GO) analysis for these genes. Similar to previous research, the increase in hematopoietic stem cell population and functional decline in age-related hematopoietic pathologies have contributed significantly. Our results further enabled identification of candidate genes that are associated with aging such as negative regulation of cellular process such protein modification and protein phosphorylation processes. A majority of the top GO genes encoded proteins function intracellularly and also provide insights into plasma membrane. Gene expression profile with GO enrichment further reveals a metabolic process of the immunopathological basis of aging that are associated with several signaling cascades which plays an important role of the family of ATP-binding cassette (ABC) transporters.

BACKGROUND

The process of aging is characterized by a degeneration in the maintenance of homeostatic processes with advancing time, leading to functional decline in a variety of organ and tissue systems and increased risk for many diseases (cardiovascular, several types of cancer, metabolic and neurological diseases) and ultimately death [1]. Aging decreases an organism’s ability to handle environmental and physiological disturbance which also another cause that increases the vulnerability to death [2]. It is important to identify and characterize the genetic and environmental factors (smoking, environmental pollution) that modulate longevity in order to understand the basic mechanism of aging. The complex aging process and wide variability between individuals limited the identification of factors affecting aging [2]. To date, several theories have been proposed which provided beneficial insights to understand the physiological changes during the aging process. The notable ones are immunologic, inflammation, free radical and mitochondrial. To date several hundred genes have been found to associated with aging.

MATERIALS AND METHODS

2.1. Microarray data and preprocessing

Expression data from human bone marrow hematopoietic stem cells were downloaded from the gene expression omnibus (GEO) database with GSE32719 was used [3]. Genomic information ranging from gene sequences to protein structure predictions were obtained. As described by Pang et al [3], these data sets contain a total of 50,000 gene expression of healthy human bone marrow hematopoietic stem cells in groups of 14 young (20–31 years), 5 middle age (42–61), 8 old (65–85) groups. The GSE32719 data set is analyzed by using the GEOquery package [4] in Bioconductor [5] following standard procedures in R studio [6]. The other packages we used in R studio are as the following; Biobase [4] and gplots [7] packages.

2.2. Screening of differentially expressed genes

We separate samples into three conditions provided that young-old , young-middle aged , and middle-old aged.  The data set was normalized by computing the means of the samples of each condition in the the R programming language. The process was performed as computing fold-change (biological significance) difference between the means of the conditions. We finally find statistical significance using t-test by taking fold cut-off value 0.075 young and old (0.05; young-middle and middle-old samples) and p-value cutoff value 0.01 for each conditions. The genes are screened based on satisfaction of the filtering criteria. We highlight the significantly up-regulated and down-regulated differential expressed genes (DEGs).

2.2. Annotation of differentially expressed genes

Expression measurements annotations for up-regulated and down regulated DEGs for each conditions probes mapped to gene names using Ensemble Biomart server [8]. We choose the database Ensemble Genes 100, filtered by genes and uniport id with the related Affy ids. All characterized genes were carefully investigated and additional components like the Universal Protein resource, and physical properties Gene Ontology (GO) and annotation types were derived using ***G****ene****O****ntology En****RI****chment ana****L****ysis and Visua****L****iz****A****tion Tool (Gorilla)*

REFERENCES

[1] M. Fraga and M. Esteller, “Fraga, M. F. & Esteller, M. Epigenetics and aging: the targets and the marks. Trends Genet. 23, 413-418,” *Trends Genet.*, vol. 23, pp. 413–418, Sep. 2007, doi: 10.1016/j.tig.2007.05.008.

[2] M. P. Rodero *et al.*, “Immune surveillance of the lung by migrating tissue monocytes,” *Elife*, vol. 4, pp. e07847–e07847, Jul. 2015, doi: 10.7554/eLife.07847.

[3] W. W. Pang *et al.*, “Human bone marrow hematopoietic stem cells are increased in frequency and myeloid-biased with age,” *Proc. Natl. Acad. Sci. U. S. A.*, vol. 108, no. 50, pp. 20012–20017, 2011, doi: 10.1073/pnas.1116110108.

[4] S. Davis and P. Meltzer, “GEOquery: A bridge between the Gene Expression Omnibus (GEO) and BioConductor,” *Bioinformatics*, vol. 23, pp. 1846–1847, Aug. 2007, doi: 10.1093/bioinformatics/btm254.

[5] R. Ihaka and R. Gentleman, “R: A Language for Data Analysis and Graphics,” *J. Comput. Graph. Stat.*, vol. 5, no. 3, pp. 299–314, Sep. 1996, doi: 10.1080/10618600.1996.10474713.

[6] R Core Team, “R: A language and environment for statistical computing and Foundation for Statistical Computing.” 2020.

[7] G. R. Warnes *et al.*, “gplots: Various R programming tools for plotting data,” *R Packag. version*, vol. 2, no. 4, p. 1, 2009.

[8] A. D. Yates *et al.*, “Ensembl 2020,” *Nucleic Acids Res.*, vol. 48, no. D1, pp. D682–D688, Nov. 2019, doi: 10.1093/nar/gkz966.