The Influence of ecDNA on HNSC and ESCA

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Abstract: ecDNA is a unique circular DNA located outside the cell chromosomes. By enriching the experimental data on the database and analyzing survival, we found that ecDNA acts on HNSC cancer species, which mainly has a huge impact on the immune system, and the survival time of the ecDNA-positive group will decline from a trend. At the same time, it was found that ecDNA may be a biological process that acts on biological proteins in ESCA cancer species.

1. Background

Extrachromosomal circularization DNA, abbreviated as ecDNA, is a type of DNA outside the chromosomes. Most DNA exists on the chromosomes, and there are many forms of DNA outside the chromosomes. This kind of DNA is a genomic feature of cancer. At present, the role of ecDNA in cancer is not well known. In this experiment, we hope to discover the role of ecDNA in some cancers through statistics of data.

Squamous cell carcinoma of the head and neck is a cancer that usually starts with squamous cells that line the surface of the mucosa of the head and neck. Head and neck cancer can form in the mouth, throat, and nasal cavity. The spread of squamous cell carcinoma of the head and neck is, almost always in the local and/or cervical lymph nodes. We hope to find the role of ecDNA in HNSC.

Esophageal cancer is a disease in which cancer cells form in the tissues of the esophagus. Smoking, heavy drinking, and Barrett's esophagus increase the risk of esophageal cancer. The signs and symptoms of esophageal cancer are weight loss and pain or difficulty swallowing. We will also study the effect of ecDNA in esophageal cancer. (U.S. Department of Health and Human Services, 2020)

2. Method

A. data processing

1. Get data: First, we download data on ESCA and HNSC from UCSC Xena. We download the HTSeq-FPKM data, and then we download the data Mu Tect2 Variant Aggregiation and masking and Curated survival data.

2. Organize and integrate data: We first import the data into Rstudio, and change the 01A in the code in the TCGA data to 01, so that we can ensure the unity of the data. Then merge the tumer data together.

3. Output data: We first organize the data into a matrix, behavioral genes, and list them as sample IDs, with ecDNA- in the front and ecDNA+ in the back. Then we transfer gene ID conversion, and finally we get a piece of information about ecDNA- and ecDNA+.

B. Difference analysis

Remove all zero samples, and then find the average of negative and positive samples. Then we use log transfer the sample and use Wilcox. Test on the transferred negative and positive samples to get the P-Value. Then using FDR method to correct the p-Value. Finally, filtering out the sample that P-Value less than 0.05 for further analysis.

C. Enrichment analysis

1. First transfer id conversion to make it the easy-to-analyze id we want,

2. Remove NA samples.

3. We use GO enrichment analysis and Kegg enrichment analysis on the samples.

D. Survive analysis

After we eliminated the data with no results, we integrated the ecDNA positive and negative survival data to form a line graph that allowed us to clearly see the probability and duration of survival.

3. Result

HNSC

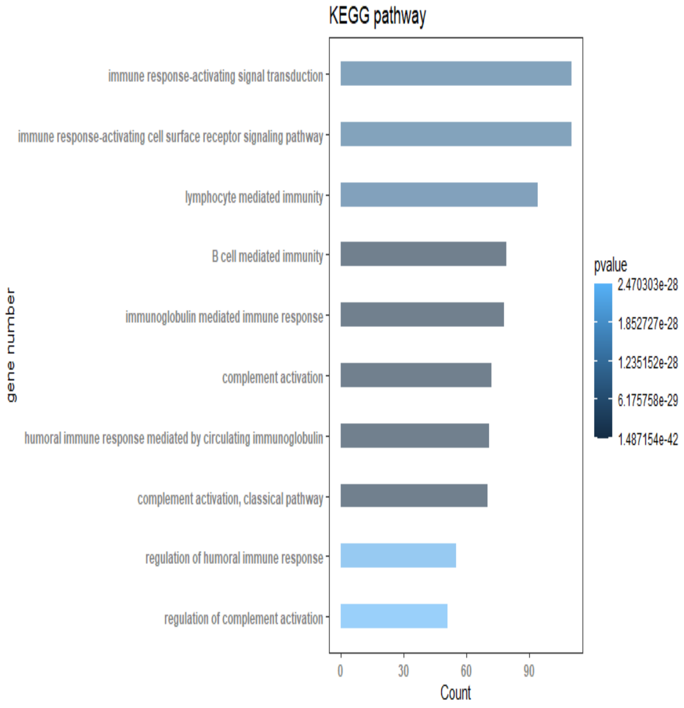

Figure 1 GO pathway result

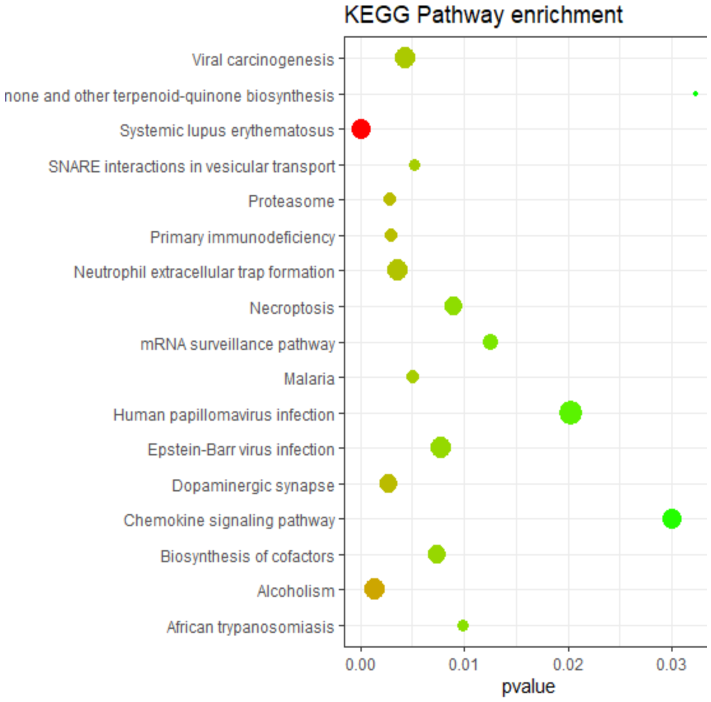

Figure 2 Kegg enrichment result

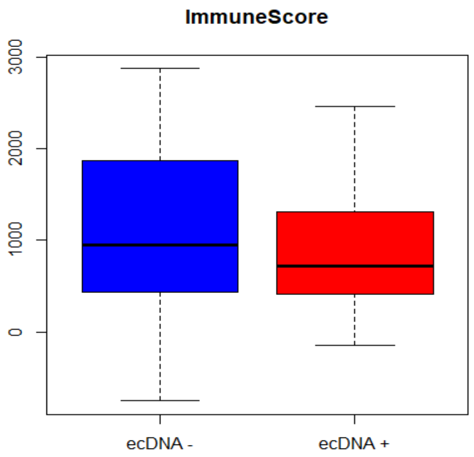

Figure 3 immune score chart

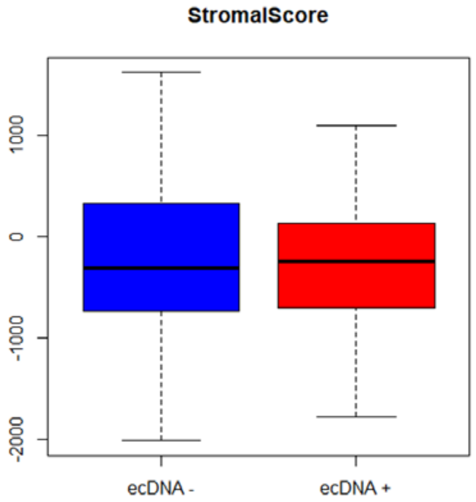

Figure 4 stormal score chart

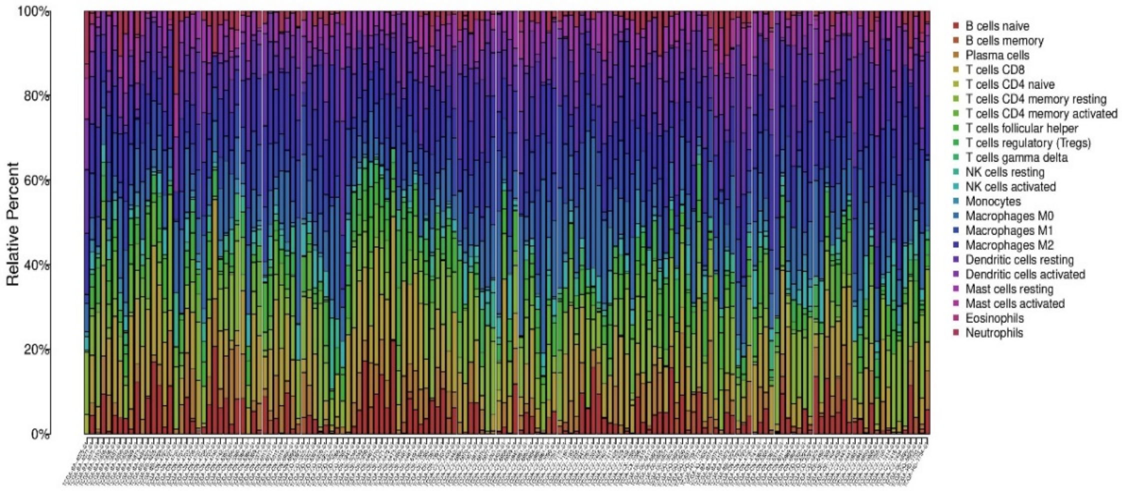

Figure 5 The proportion of different immune cells related

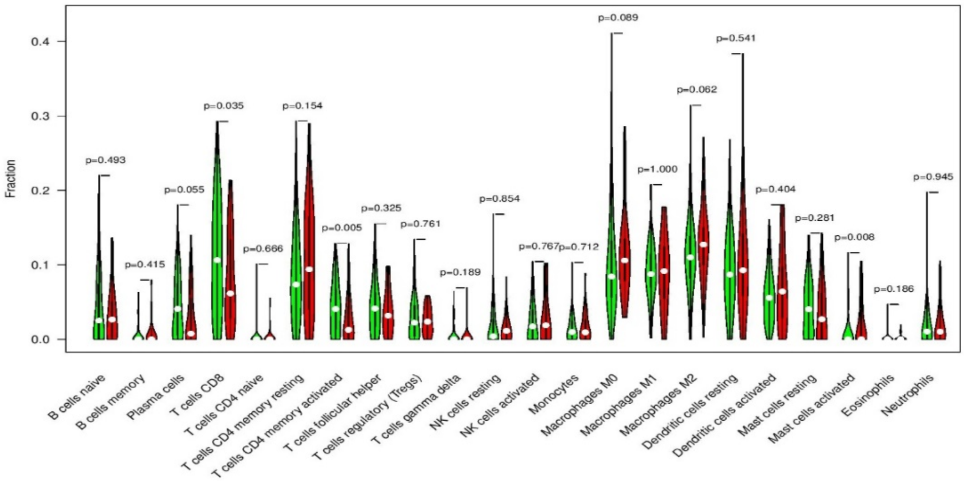

Figure 6 Correlation diagram between different immune cells and eDNA

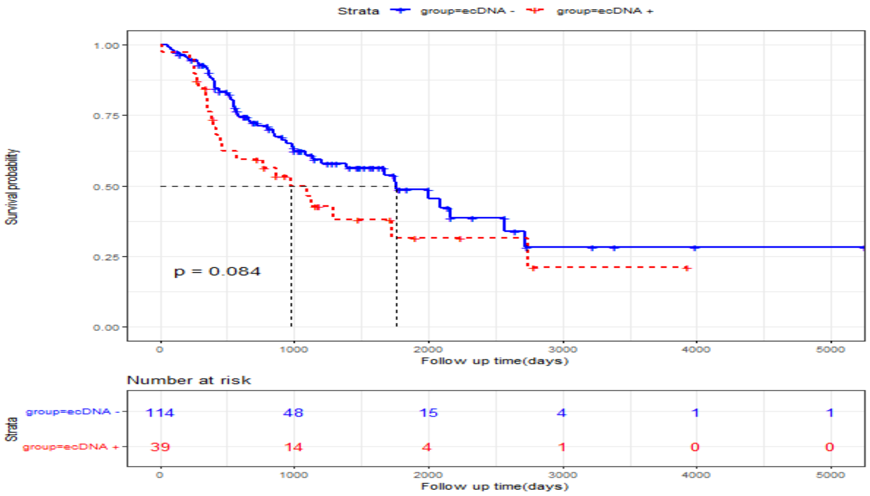

Figure 7 Survival Analysis Chart of HNSC

ESCA

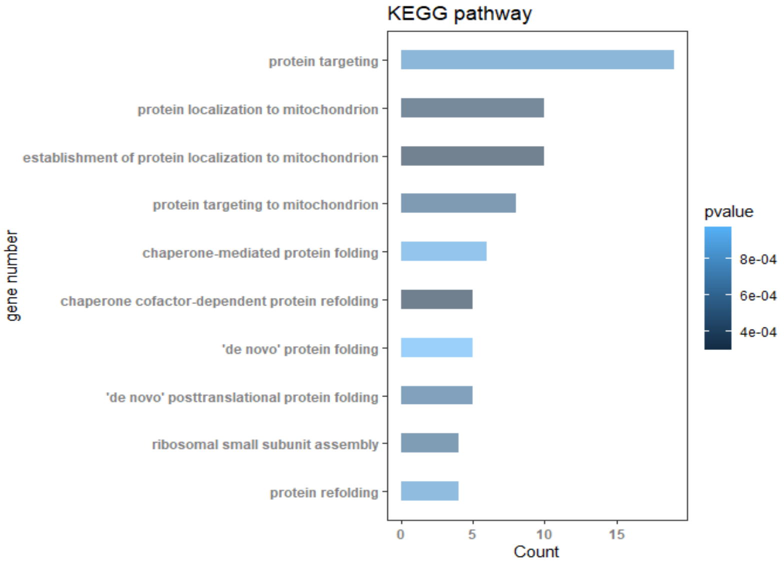

Figure 8 GO pathway result

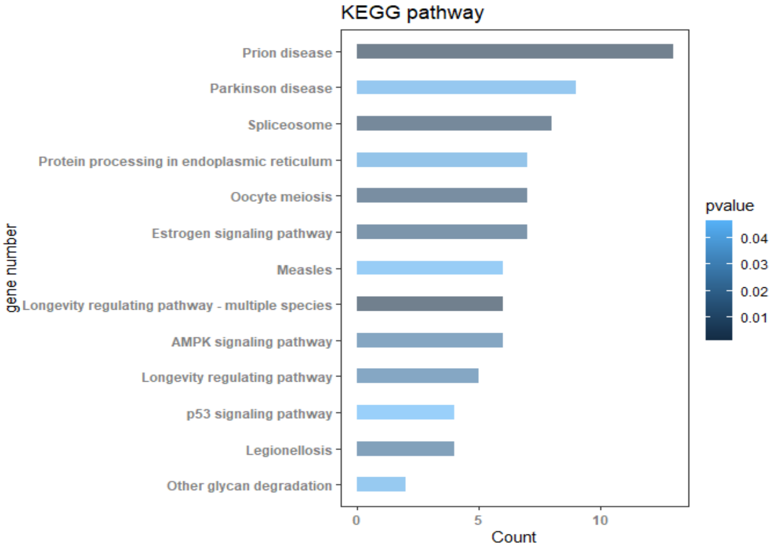

Figure 9 Kegg enrichment result

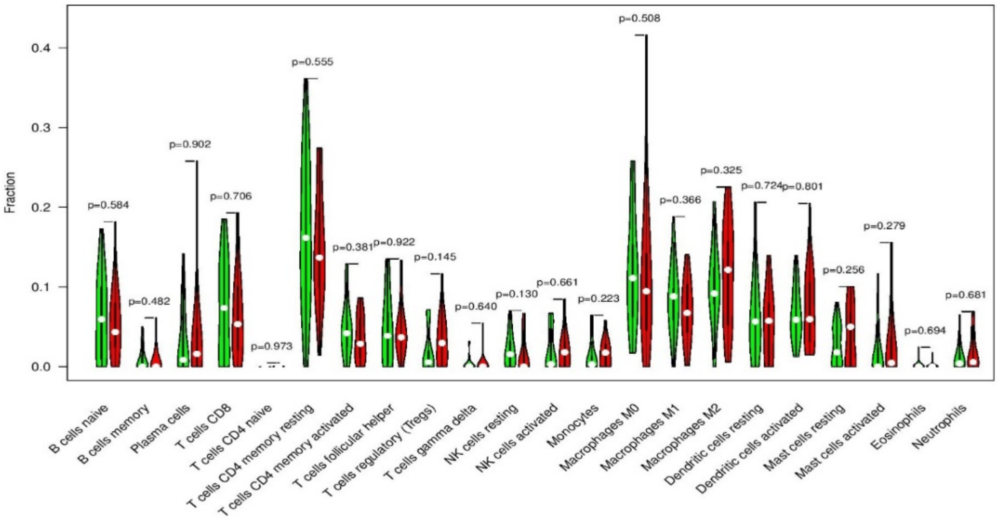

Figure 10 Correlation diagram between different immune cells and eDNA

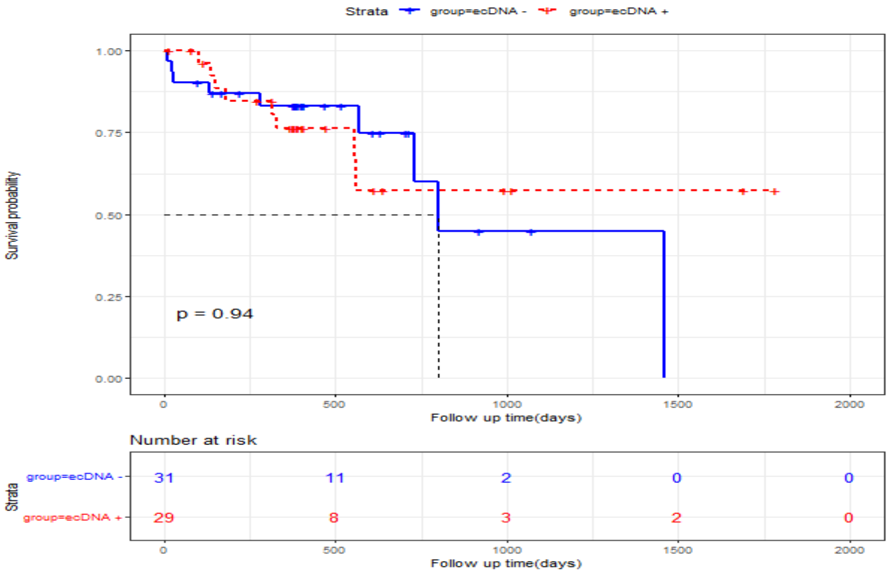

Figure 11 Survival Analysis Chart of ESCA

4. Conclusion

HNSC

- Through the analysis of the experimental results, we can find that ecDNA acts on HNSC cancer, which mainly has a huge impact on the immune system. In the GO enrichment analysis, we can see from the BAR diagram that most of the important functions of HNSC affected by ecDNA are related to the immune system. HNSC is a highly immunodeficient tumor (Yueming Zhang, 2020). When squamous cell carcinoma of the head and neck spreads, it almost always spreads to the local and/or neck lymph nodes. This also verified that the function of ecDNA mainly affects the immune system, which in turn leads to cancer.
- In the kegg bubble chart, we can see that there are more ecDNAs associated with viruses than viruses, and we can know that the positive expression of ecDNA in HNSC is more likely to be caused by viruses. And the survival individuals in the ecDNA-positive group tend to be less than those in the negative group.
- In the immune score chart, we calculated a p-value of 0.2309. Although it exceeds the value of 0.05, because this value is relatively small, ecDNA is still related to immunity.
- In the stromal score chart, we calculated a p-value of 0.9529. There is no significant difference between ecDNA- and ecDNA+ in this respect, so ecDNA may have no effect in this respect.
- Among 22 immune cells, the P value of T cell CD4 memory activation and mast cell resting is less than 0.05. However, the negative group of ecDNA was higher than the positive group. The P value of the positive group is higher than that of the negative group is greater than 0.05, the calculation result is not credible.
- In the survival analysis, although its P-Value is greater than 0.05, it does not exceed that much. It can be seen from the figure that the overall trend is that the survival of the negative group is better than the positive group. It can be concluded that individuals who are negative for ecDNA are more likely to survive.

ESCA

- Through GO analysis, ESCA is mainly related to protein targeting, and the relationship between protein and mitochondria is related to protein folding.
- Through the analysis in the Kegg diagram, we can see that ESCA can be produced by viruses, diseases, and some biological processes.
- From the figure, we can see that the positive and negative ecDNAs of ESCA have almost no correlation with immune cells.
- The P value is significantly greater than 0.05. From the survival analysis, it is difficult to see the relationship between negative and positive ecDNA and survival.
- Through the analysis of the experimental results, we can find that ecDNA may be a biological process that acts on biological proteins in ESCA cancer species. There is no evidence that ecDNA acts on the immune system. No significant difference in survival between negative and positive groups was found

References

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