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# Long non-coding RNAs as potential prognostic biomarkers in gastric cancer

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# Introduction

Gastric cancer (GC) is the fourth cause of cancer related death in the world. GC has a poor prognosis and new biomarkers to predict the prognosis of patients are needed. Long non-coding RNAs (lncRNAs) are a group of non-coding RNAs which can be utilized for this purpose. Because of having high specificity and existing in different tissues and fluids of body, lncRNAs have attracted attentions. lncRNAs are differentially expressed in GC and have vital roles in formation and progression of GC. The aim of this study is identification of differentially-expressed lncRNAs (DELs) in GC, between cancerous and paracancerous tissues and their correlation with prognosis in GC.

# Materials and Methods

RNA-seq data of GC from 375 cancerous and 32 paracancerous GC tissue samples were retrieved from The Cancer Genome Atlas (TCGA) database, using TCGAbiolinks package in RStudio software. The correlations between samples were examined by TCGAbiolinks package. Then, data were normalized by DESeq2 package and differentially expressed RNAs (DERs) were identified. biomaRt package was utilized for annotation of DERs and DELs were identified. Clinical data of the samples were retrieved from TCGA by TCGAbiolinks package and the prognostic values of DELs were evaluated by survival package in RStudio (based on Kaplan-Meier method). lncRNAs correlating with survival in GC (Hazard Ratio (HR) $\neq 1$ and p-value $< 0.05$), were identified and survival plots of six lncRNAs with HR $> 1.5$ and p-value $< 0.05$, were shown.

# Results

The correlation of samples were verified and all samples had spearman correlation more than 0.7 with the others. Based on adjusted p-value < 0.001 and |logFC| > 4, 344 differentially expressed RNAs (DERs) between cancerous and paracancerous GC tissues were identified. Among them, 99 lncRNAs including 91 upregulated and eight downregulated, existed. Survival analysis revealed 18 lncRNAs which have correlation with prognosis of GC according to HR > 1 and p-value < 0.05 (**Table 1**). In fact, there is a revers correlation between their expression and survival of GC patients. Six lncRNAs (*LINC00392*, *LINC01194*, *AC011352.1*, *AC093895.1*, *AC090809.1* and *LINC02864)* had HR > 1.5 (**Figure 1**). Furthermore, the expression of two lncRNAs (*LINC01210 and AC007159.1)* based on HR < 1 and p-value < 0.05 correlate with the prognosis of GC patients, directly.

# Discussion

Different studies have delt with the role of lncRNAs as prognostic biomarkers in GC. The correlation between the expression of lncRNAs with survival of GC patients can be direct or indirect. lncRNAs such as *H19*, *HOTAIR* and *PVT1* have been identified as potential prognostic biomarkers in GC. These studies introduce new and better prognostic biomarkers in GC which can be used in near future to predict the survival of these patients more precisely.

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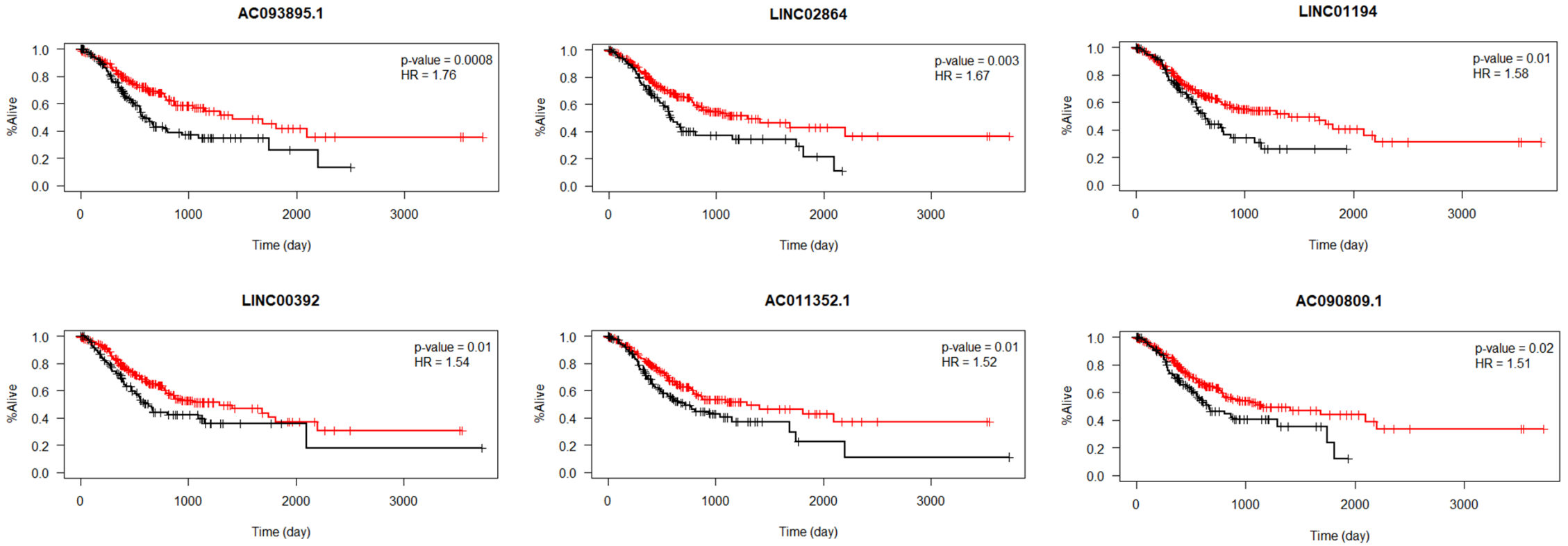
# Table 1: lncRNAs associating with survival in GC

| lncRNA | Group | Number of patients | Hazard Ratio | p-value |
|---|---|---|---|---|
| *AC093895.1* | Low<br>High | 205<br>165 | 1.76 | 0.0008 |
| *LINC02864* | Low<br>High | 255<br>115 | 1.67 | 0.003 |
| *LINC01194* | Low<br>High | 253<br>117 | 1.58 | 0.01 |
| *LINC00392* | Low<br>High | 254<br>116 | 1.54 | 0.01 |
| *AC011352.1* | Low<br>High | 224<br>146 | 1.52 | 0.01 |
| *AC090809.1* | Low<br>High | 236<br>134 | 1.51 | 0.02 |
| *POU6F2-AS2* | Low<br>High | 233<br>137 | 1.49 | 0.02 |
| *LINC01614* | Low<br>High | 183<br>187 | 1.49 | 0.02 |
| *LINC02830* | Low<br>High | 235<br>135 | 1.49 | 0.02 |
| *AL139002.1* | Low<br>High | 247<br>123 | 1.48 | 0.03 |
| *AL139023.1* | Low<br>High | 239<br>131 | 1.48 | 0.02 |
| *AC022031.2* | Low<br>High | 256<br>114 | 1.45 | 0.03 |
| *MAGEA4-AS1* | Low<br>High | 263<br>107 | 1.44 | 0.04 |
| *AC106875.1* | Low<br>High | 227<br>143 | 1.43 | 0.03 |
| *LINC00355* | Low<br>High | 234<br>136 | 1.43 | 0.04 |
| *DSCR8* | Low<br>High | 257<br>113 | 1.43 | 0.04 |
| *LINC01980* | Low<br>High | 229<br>141 | 1.42 | 0.04 |
| *AC113346.1* | Low<br>High | 206<br>164 | 1.41 | 0.04 |

# Figure 1: Six survival-related lncRNAs with hazard ratio > 1.5



# Conclusion

These lncRNAs can be utilized as potential prognostic biomarkers in GC in the future. Further investigations are needed to unravel the precise correlation of these lncRNAs with the prognosis of GC.

# References

Colaprico, A., Silva, T. C., Olsen, C., Garofano, L., Cava, C., Garolini, D., . . . Noushmehr, H. (2015). TCGAbiolinks: an R/Bioconductor package for integrative analysis of TCGA data. *Nucleic Acids Research, 44*(8), e71-e71. doi:10.1093/nar/gkv1507

Durinck, S., Spellman, P. T., Birney, E., & Huber, W. (2009). Mapping identifiers for the integration of genomic datasets with the R/Bioconductor package biomaRt. *Nature protocols, 4*(8), 1184-1191. doi:10.1038/nprot.2009.97

Gao, Y., Wang, J.-W., Ren, J.-Y., Guo, M., Guo, C.-W., Ning, S.-W., & Yu, S. (2020). Long noncoding RNAs in gastric cancer: From molecular dissection to clinical application. *World journal of gastroenterology, 26*(24), 3401-3412. doi:10.3748/wjg.v26.i24.3401

Love, M. I., Huber, W., & Anders, S. (2014). Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. *Genome Biology, 15*(12), 550. doi:10.1186/s13059-014-0550-8

Machlowska, J., Baj, J., Sitarz, M., Maciejewski, R., & Sitarz, R. (2020). Gastric Cancer: Epidemiology, Risk Factors, Classification, Genomic Characteristics and Treatment Strategies. *International journal of molecular sciences, 21*(11), 4012. doi:10.3390/ijms21114012

Nasrollahzadeh-Khakiani, M., Emadi-Baygi, M., Schulz, W. A., & Nikpour, P. (2016). Long noncoding RNAs in gastric cancer carcinogenesis and metastasis. *Briefings in Functional Genomics, 16*(3), 129-145. doi:10.1093/bfgp/elw011

Zhu, M., Wang, Y., Liu, X., Wen, X., Liang, C., & Tu, J. (2017). LncRNAs act as prognostic biomarkers in gastric cancer: A systematic review and meta-analysis. *Frontiers in Laboratory Medicine, 1*(2), 59-68. doi:https://doi.org/10.1016/j.flm.2017.05.003

Fattahi S, Kosari-Monfared M, Golpour M, Emami Z, Ghasemiyan M, Nouri M, et al. LncRNAs as potential diagnostic and prognostic biomarkers in gastric cancer: A novel approach to personalized medicine. Journal of cellular physiology. 2020;235(4):3189-206.