Novel gene signatures for prediction of preeclampsia in second-trimester amniotic fluid

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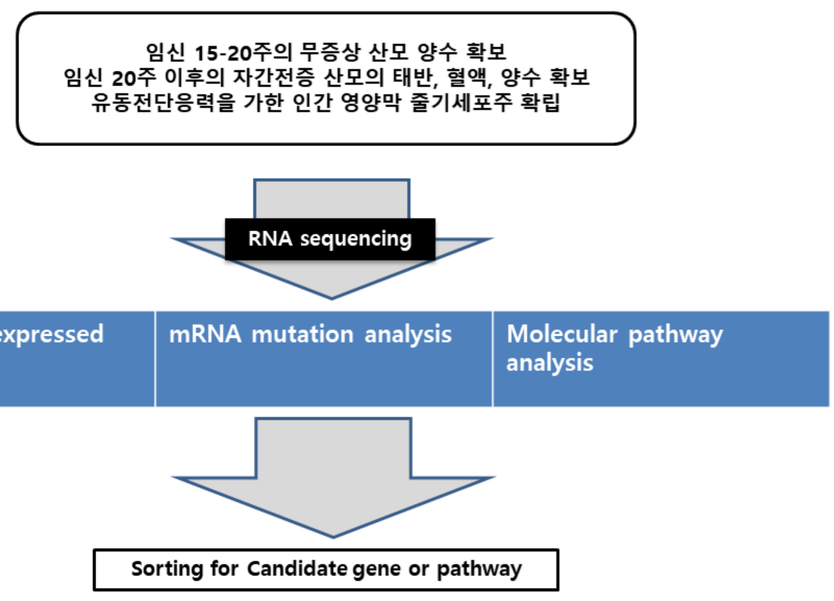
Objectives

Preeclampsia is a major disease in 5-10% of all pregnancies that increases maternal and fetal mortality and morbidity during pregnancy, but has not shown a significant decrease despite continuous medical advances. In this study, RNA sequencing is used to discover markers that can predict future preeclampsia in the amniotic fluid of asymptomatic mothers in the second trimester (15-20 weeks of gestation).



Materials and Methods

Amniotic fluid is collected from 16 asymptomatic mothers in the second trimester of pregnancy (15-20 weeks of pregnancy), and total RNA is extracted after confirming the occurrence of preeclampsia. Libraries were prepared from total RNA using the NEBNext Ultra II Directional RNA-Seq Kit. High-throughput sequencing was performed as paired-end 100 sequencing using NovaSeq 6000 (Illumina, Inc., USA). A quality control of raw sequencing data was performed using FastQC (Simon, 2010) and the RC (Read Count) data were processed based on FPKM+Geometric normalization method using EdgeR within R (R development Core Team, 2020).

Results

As a result of RNA sequencing, there were 39 differentially expressed genes (DEGs) between normal mothers and preeclampsia mothers (fold change 1.5 or more, p-value less than 0.5). The number of down-regulated genes was 18. The up-regulated genes with more than 2 fold were ABCG1, KRT24, SPRR2F and BOLA1, and expression decreased by 0.5 fold or less were SNORA27 and FAM193. By Gene Category Chart analysis, these genes were confirmed to be related to oxidative stress, estrogen receptor signaling and hypoxia signaling pathway.

Conclusions

We have discovered 39 differentially expressed genes, and it is necessary to confirm the role of these genes as predictive markers of preeclampsia through amniocentesis..

Table 1. 39 differentially expressed genes (DEGs) between normal mothers and preeclampsia mothers (fold change 1.5 or more, p-value less than 0.5).

Gene symbol	Fold change	p-value
ABCG1	8.238	0.000
KRT24	3.004	0.000
SPRR2F	2.618	0.008
BOLA1	2.182	0.021
MT1H	1.872	0.030
SPRR2D	1.755	0.000
SULT1A1	1.753	0.010
SPRR2A	1.741	0.000
CYP26B1	1.718	0.000
CDKN2AIP	1.691	0.002
IGFBP3	1.675	0.001
HOOK2	1.636	0.001
AGTRAP	1.630	0.029
SPRY2	1.628	0.011
FAM25A	1.626	0.038
CXorf40B	1.621	0.032
TACSTD2	1.610	0.003
CYP2W1	1.572	0.012
PSMB10	1.568	0.030
FOS	1.542	0.006
CRCT1	1.522	0.003
MTRNR2L2	1.513	0.005
LOC100129434	0.650	0.042
APOA1	0.646	0.036
PARP15	0.641	0.035
ABCC9	0.631	0.027
SLC26A3	0.625	0.007
TMEM45A	0.624	0.031
LOC101926898	0.623	0.019
MAB21L3	0.619	0.007
APOB	0.610	0.001
LINC00506	0.588	0.003
COMMD10	0.584	0.014
DBET	0.577	0.000
CNIH4	0.566	0.004
C11orf72	0.524	0.003
POLR3K	0.511	0.010
FAM193B	0.429	0.000
SNORA27	0.007	0.028

Figure 1. Gene Category Chart analysis

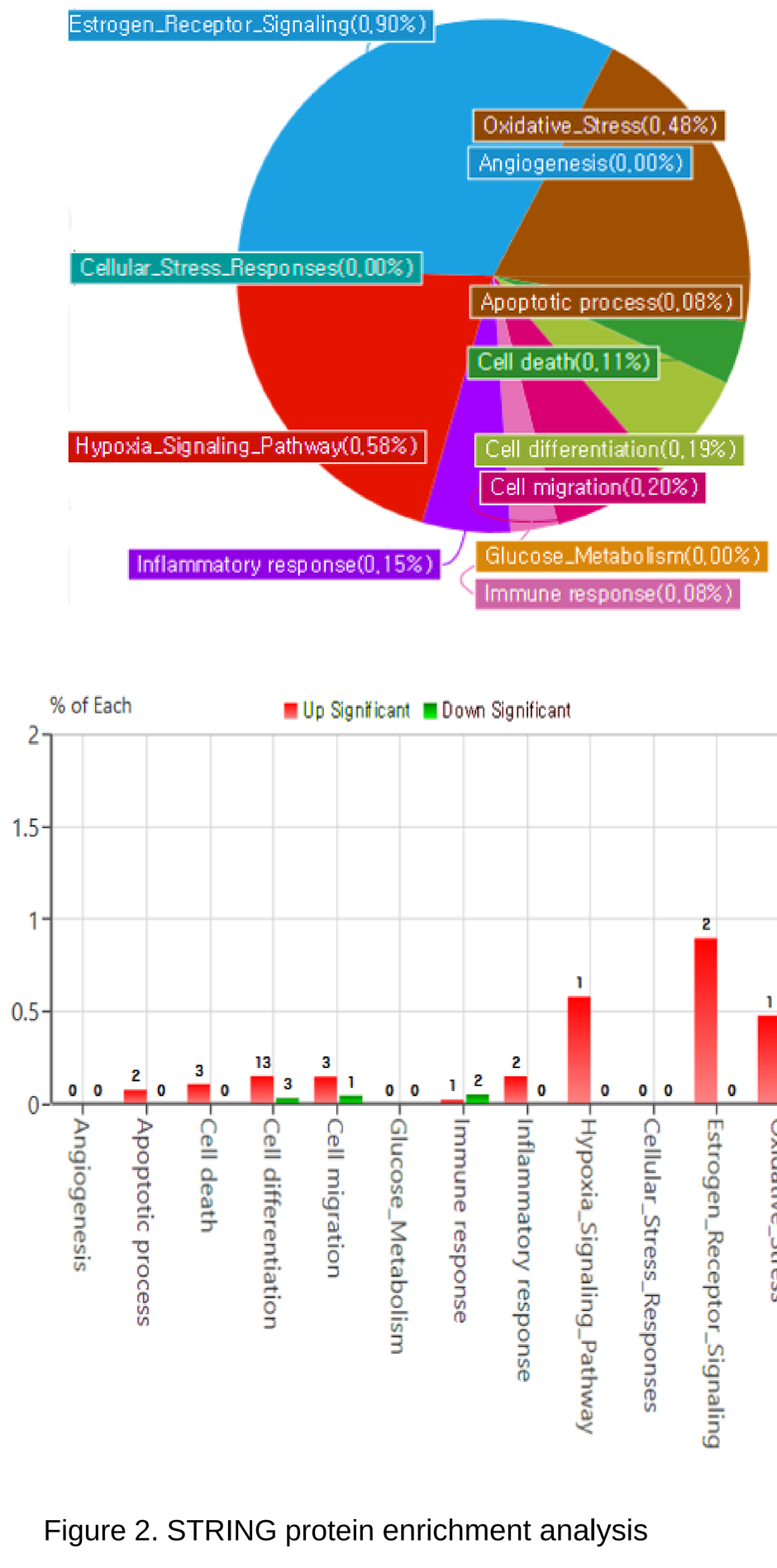


Figure 2. STRING protein enrichment analysis