Gene 591 (2016) 471–477

Contents lists available at ScienceDirect

Gene

journal homepage: www.elsevier.com/locate/gene

Research paper

Co-expression networks revealed potential core lncRNAs in the triple-negative breast cancer

Fan Yang [a,1], Ye-huan Liu [a,1], Si-yang Dong [a], Zhi-han Yao [a], Lin Lv [a], Rui-min Ma [a], Xuan-xuan Dai [a], Jiao Wang [b], Xiao-hua Zhang [a,*], Ou-chen Wang [a,*]

[a] Department of Surgical Oncology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, PR China
[b] Eye Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, PR China

ARTICLE INFO

Article history:
Received 19 March 2016
Received in revised form 26 April 2016
Accepted 1 July 2016
Available online 2 July 2016

Keywords:
Triple-negative breast cancer
Long non-coding RNA
RMST
Expression profile

ABSTRACT

Triple-negative breast cancer (TNBC) is an aggressive type of breast cancer with unfavorable outcome. It is urgent to explore novel biomarkers and potential therapeutic targets in this malignancy. Increasing knowledge of long noncoding RNAs (lncRNAs) significantly deepens our understanding of cancer biology. Here, we sequenced eight paired TNBC tumor tissues and non-cancerous tissues, and validated significantly differentially expressed lncRNAs. Gene ontology (GO) and pathway analysis were used to investigate the function of differentially expressed mRNAs. Further, potential core lncRNAs in TNBC were identified by co-expression networks. Kaplan-Meier analysis also indicated that breast cancer patients with lower expression level of rhabdomyosarcoma 2 associated transcript (RMST), one of the potential core lncRNAs, had worse overall survival. To the best of our knowledge, it was the first report that RMST was involved in breast cancer. Our research provided a rich resource to the research community for further investigating lncRNAs functions and identifying lncRNAs with diagnostic and therapeutic potentials in TNBC.

1. Introduction

Breast cancer is the leading cause of cancer mortality among women worldwide.

(Siegel et al., 2015). Triple-negative breast cancer (TNBC) is characterized by lacking of expression of hormone receptor as well as human epidermal growth factor receptor 2 (Her-2) so that patients could not benefit from both endocrine therapy and Her-2 targeted therapy(Lehmann et al., 2011; Agrawal and Mayer, 2014). Compared to other subtypes of breast cancer, TNBC patients have higher rates of distant metastasis and worse prognosis (Bosch et al., 2010). It is urgent to understand the initiation and developmental mechanisms of TNBC.

Long noncoding RNAs (lncRNAs) are RNA transcripts longer than 200 nt without protein coding capacity (Kung et al., 2013). Based on genomic position to protein-coding genes, lncRNAs can be classified into five groups: sense, antisense, bidirectional, intronic and intergenic (Ponting et al., 2009). Accumulating evidence indicates that lncRNAs are involved in the initiation and progression of cancer rapidly. Aberrant expression levels of lncRNAs are associated with various malignant biological processes, including tumorigenesis, proliferation, migration, and metastasis (Prensner and Chinnaiyan, 2011; Spizzo et al., 2012).

Recently, Shen et al. and Chen et al. have reported a set of dysregulated lncRNA between TNBC and paired normal tissues (Shen et al., 2015; Chen et al.,2015). However, it is challenging to identify core onco-lncRNAs among the vast dysregulated lncRNAs. In this study, we aimed to reveal potential core lncRNAs in TNBC by co-expression networks, which might be helpful to offer therapeutic targets for clinical treatment or potential biomarkers for diagnosis.

2. Material and methods

2.1. Patient samples and ethical standards

The study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. Informed consent was

Abbreviations: TNBC, triple-negative breast cancer; LncRNA, long non-coding RNA; HER-2, human epidermal receptor 2; FDR, false discovery rate; FC, Fold Change; GO, Gene ontology; RMST, rhabdomyosarcoma 2 associated transcript; TCGA, The Cancer Genome Atlas; DEGs, differentially expressed genes; KEGG, Kyoto Encyclopedia of Genes and Genomes; qRT-PCR, Quantitative real-time polymerase chain reaction; SOX2, Sex determining region Y-box 2.

* Corresponding authors.
E-mail addresses: xiaohuazhang2015@sina.com (X. Zhang), woconcology2000@163.com (O. Wang).

[1] Fan Yang and Ye-huan Liu contributed equally to this work.

http://dx.doi.org/10.1016/j.gene.2016.07.002
0378-1119/

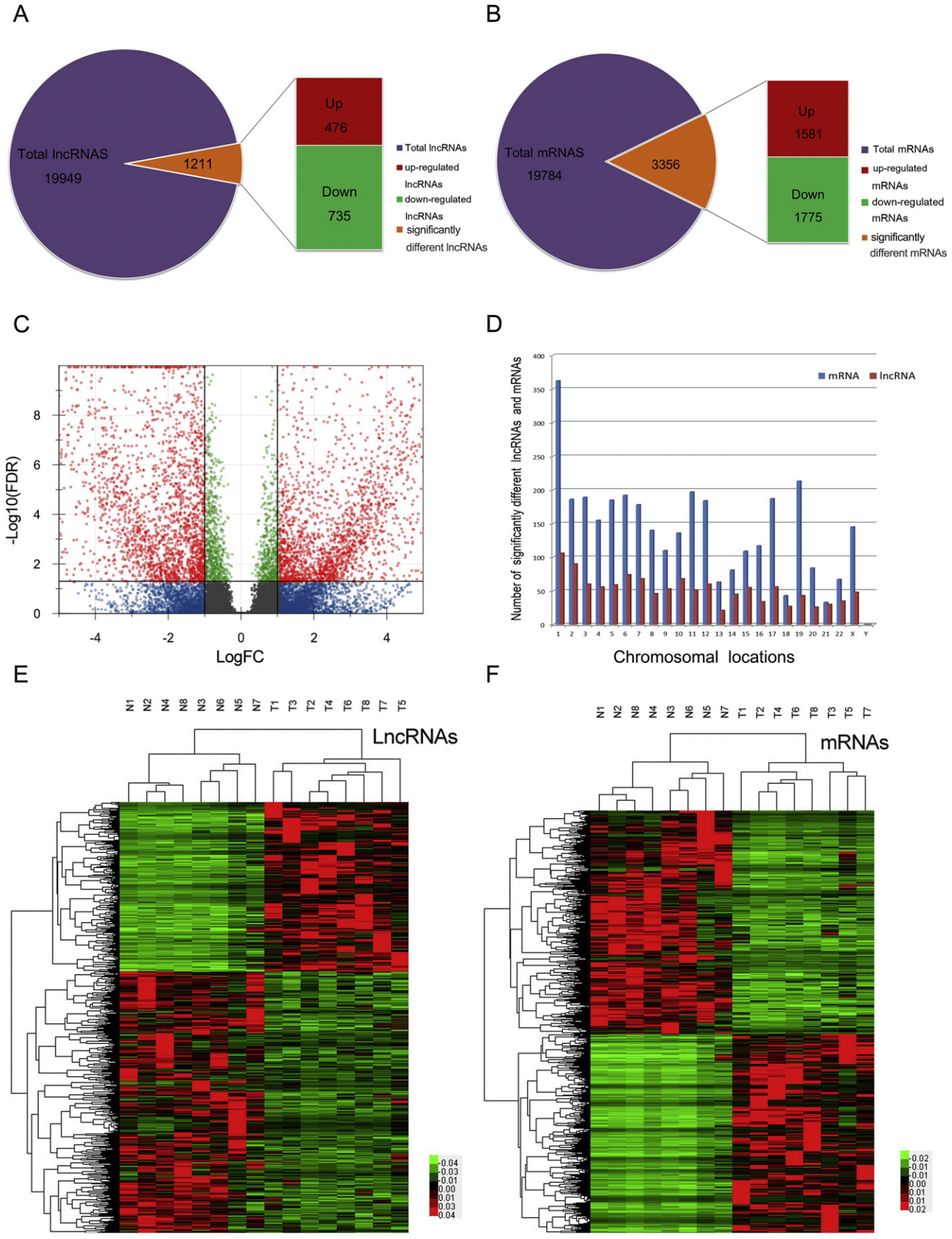

Fig. 1. Dysregulated RNA expression profiles in TNBC. (A, B) Pie charts showing the distribution of dysregulated lncRNAs and mRNAs according to RNA-seq. (C) Volcano plot showing variation in gene expression. The negative log of FDR (base 10) is plotted on the y-axis, and the log of the FC (base 2) is plotted on the x-axis. (D) Chromosomal locations of each of the significantly altered lncRNAs and mRNAs. (E, F) Heatmaps of differentially expressed lncRNAs and mRNAs in tumor and adjacent normal tissues.