Genomics Data 5 (2015) 228–230

Contents lists available at ScienceDirect

Genomics Data

journal homepage: http://www.journals.elsevier.com/genomics-data/

Data in Brief

Transcriptomic profiling comparison of YAP over-expression and conditional knockout mouse tooth germs

Ming Liu, Xiu-Ping Wang *

Department of Developmental Biology, Harvard School of Dental Medicine, Boston, MA 02115, USA

ARTICLE INFO

Article history:
Received 8 May 2015
Received in revised form 28 May 2015
Accepted 28 May 2015
Available online 4 June 2015

Keywords:
YAP
Hox
Wnt
Laminin
RNA-seq

ABSTRACT

To identify the downstream target genes of YAP, we used RNA-Seq technology to compare the transcriptomic profilings of *Yap* conditional knockout (*Yap* CKO) and *YAP* over-expression mouse tooth germs. Our results showed that some Hox, Wnt and Laminin family genes had concurrent changes with YAP transcripts, indicating that the expression of these genes may be regulated by YAP. Here, we provide the detailed experimental procedure for the transcriptomic profiling results (NCBI GEO accession number GSE65524). The associated study on the regulation of *Hoxa1* and *Hoxc13* genes by YAP was published in Molecular Cellular Biology in 2015 [Liu et al., 2015].

Specifications	
Organism/cell line/tissue	Mouse/tooth germ tissues at embryonic day 14.5
Sex	Not applicable
Sequencer or array type	Illumina Hiseq2000
Data format	Raw data: FASTQ files. Analyzed data: SOFT, MINIML, and TXT files.
Experimental factors	YAP over-expression, YAP conditional knockout and corresponding wild type controls
Experimental features	Transcriptomic profiling of YAP over-activation and conditional knockout embryonic tooth germs was compared to explore differentially expressed genes.
Consent	Not applicable

1. Direct link to deposited data

http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE65524.

2. Experimental design, materials and methods

2.1. Animal usage

The human keratin 14 promoter (K14) was used to either conditionally knockout *Yap* or drive *YAP* transgenic over-expression in mouse embryonic ectoderm-derived epithelial tissues. *Yap* conditional knockout (CKO) embryos were generated through crossing $Yap^{fl/fl}$ mice with *K14-Cre* mice [1,2] in C57BL/6 background. *YAP* over-expression (OE) embryos were generated through breeding *Col-TetO-YAP*^{S127A} mice with *K14-rtTA* mice [1–5] in FVB/NJ background, in which the constitutively active form of human YAP1 protein with the Ser127Ala mutation was over-expressed upon Doxycycline (Dox) administration. 2 mg/ml of Dox in drinking water was given starting from embryonic days 9.5 (E9.5) to E14.5. All mouse studies were performed in compliance with the protocols approved by the Harvard University Institutional Animal Care and Use Committee.

2.2. E14.5 embryonic tooth germ dissection, collection and RNA preparation

Three *Yap* CKO embryos at E14.5, along with the three corresponding three litter controls, were used for tooth germ collection of the *Yap* CKO group. Similarly, three *YAP* over-expression and three corresponding litter control embryos at E14.5 were used for the *YAP* OE group. The tooth germs in lower jaws were collected under microscopic dissection. The tooth germs were sequentially broken down by 18, 21 and 25 gauge needles in TRIzol (Life Technologies). Then total RNA was extracted and purified using RNAeasy Mini Kit (Qiagen) with on-column DNase (Qiagen) digestion, and evaluated by the Agilent 2100 bioanalyzer (Agilent Technologies, CA). The RNA integrity numbers of all 12 samples were 10 (Fig. 1), indicating high quality of the RNA samples. To minimize the individual difference from embryos, each RNA-Seq sample was pooled from the three biologically different E14.5 tooth germs with the same amount of total RNA.

* Corresponding author. Tel.: +1 617 953 2289.
E-mail address: xiuping.wang@tufts.edu (X.-P. Wang).

http://dx.doi.org/10.1016/j.gdata.2015.05.038

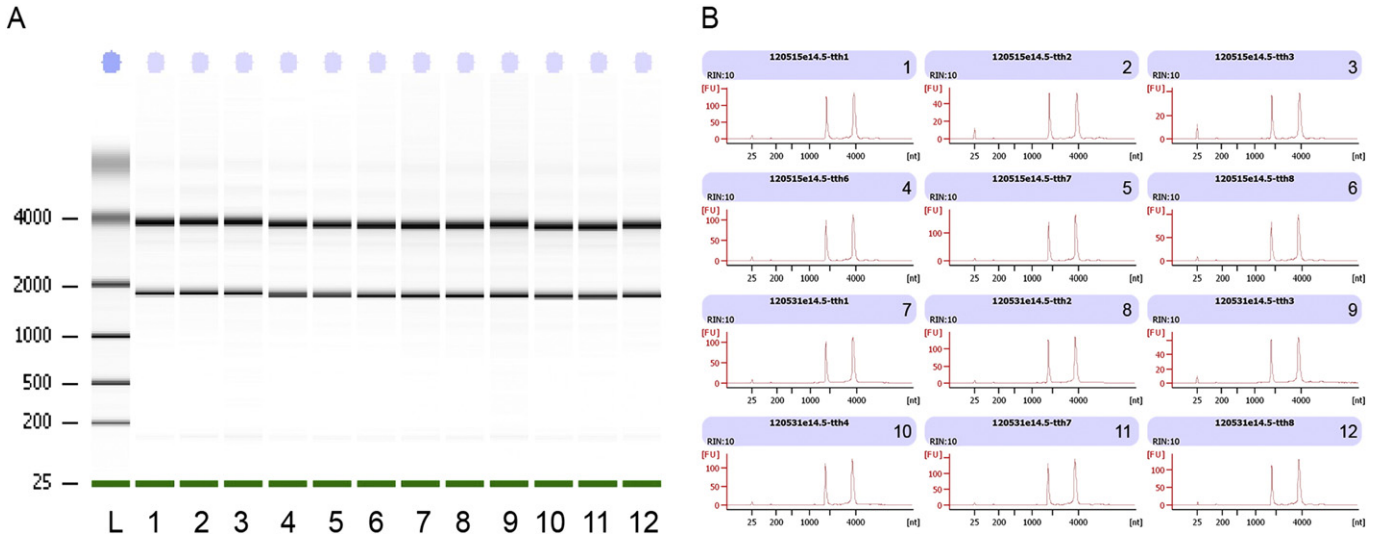

Fig. 1. Quality control of the total RNA samples of *Yap* CKO and *YAP* OE tooth germs. (A) Electrophoresis of the total RNA samples. (B) RNA integrity numbers of the total RNA samples. The *Yap* CKO samples: 1, 2 and 3; the *Yap* CKO control samples: 6, 7 and 8; the *YAP* OE samples: 7, 11 and 12; the *YAP* OE control samples: 8, 9 and 10.

2.3. RNA-sequencing

RNA-sequencing was performed on an illumina HiSeq 2000 by the Biopolymers Facility at Harvard Medical School. Paired end 50-nt sequencing strategy was used for all the RNA-Seq samples to minimize sequencing reading errors.

2.4. Data analysis

Mus musculus genome (mm9) and DNAnexus software were used to extract sequencing reads of genes from the RNA-Seq raw data. RNA-Seq raw sequencing reads and aligned reads are available through the Gene Expression Omnibus at the accession number of GSE65524. After RNA-Seq reads were extracted and aligned with the mm9 genome, the relative read ratio of each gene was calculated and further analysis was conducted. We compared the transcriptomic profilings between the *Yap* CKO and wild type tooth germs, as well as those between the *YAP* OE and wild type mouse tooth germs. In comparison with the corresponding controls at the 1.5-fold change cutoff, there were 968 down-regulated genes and 979 up-regulated genes in *Yap* CKO tooth germs, while there were down-regulated 1289 genes and up-regulated 774 genes in *YAP* over-expression tooth germs (Fig. 2). Further analysis revealed many differentially expressed genes between *Yap* CKO and *YAP* OE tooth germs. Interestingly, we found that some genes in the Hox, Wnt and Laminin families were differentially expressed in the two kinds of the tooth germs. The transcription levels of several Hox gene family members were decreased in *Yap* CKO tooth germs while their expression levels were increased in *YAP* OE tooth germs (Fig. 3), indicating that these genes could be potential downstream targets of YAP in vivo. The regulation of the *Hoxa1* and *Hoxc13* gene expression by YAP was further validated and functionally analyzed in both mouse and human epithelial cells [1].

Similar to the expression changes of the Hox genes, several Wnt and Laminin family members also showed concurrent changes with YAP transcripts (Fig. 3), although the members of these two gene families do not have a linear genomic arrangement pattern. The members of the Wnt family showing concurrent changes include Wnt10b, Wnt16, Wnt3, Wnt3a, Wnt4, Wnt6, Wnt7a and Wnt9b. The transcript levels of the latter six Wnt genes were further validated by qPCR in both tooth germs and skin samples. The qPCR results were consistent with those from RNA-Seq results. The members of the Laminin gene family with concurrent changes consist of Lama3, Lama5, Lamb3 and Lamc2.

3. Discussion

In this study, we used RNA-Seq analysis to compare the transcriptomic profilings of *Yap* CKO and *YAP* over-expression mouse tooth germs. We found that some genes in the Hox, Wnt and Laminin families exhibiting concurrent changes with YAP transcripts and may be potentially targets of YAP. The regulation of *Hoxa1* and *Hoxc13* genes by YAP was further validated and functionally analyzed in different epithelial cells of mouse tooth germs, skin samples and human keratinocytes [1].

The transcriptomic profiling comparison revealed that *Hoxa1*, *Hoxa2*, *Hoxa3*, *Hoxa5*, *Hoxb9*, *Hoxc13*, *Hoxc4*, *Hoxc8* and *Hoxd1* have differential expression in *Yap* CKO and *YAP* OE tooth germs. However, our qPCR results showed that only *Hoxa1* and *Hoxc13* had significant concurrent changes in their transcripts. This discrepancy could be due to low abundance of the Hox genes in mouse tooth tissues, which may cause high relative ratios.

Previous studies demonstrated that Wnt/β-catenin signaling regulates YAP expression in vitro [6,7]. However, how YAP affects the Wnt family members remains unknown. There are also some other gene families showing concurrent transcript changes with YAP transcripts, such as the Laminin, Rho GTPas activating protein and Ras-related

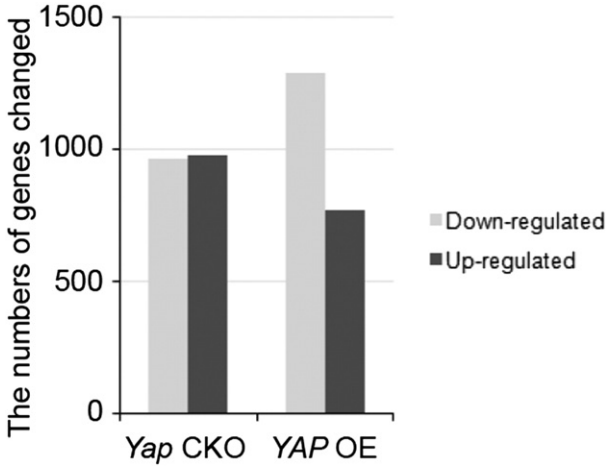

Fig. 2. The down-regulated and up-regulated gene numbers in the *Yap* CKO and *YAP* OE tooth germs at the 1.5-fold cutoff in the RNA-Seq data.

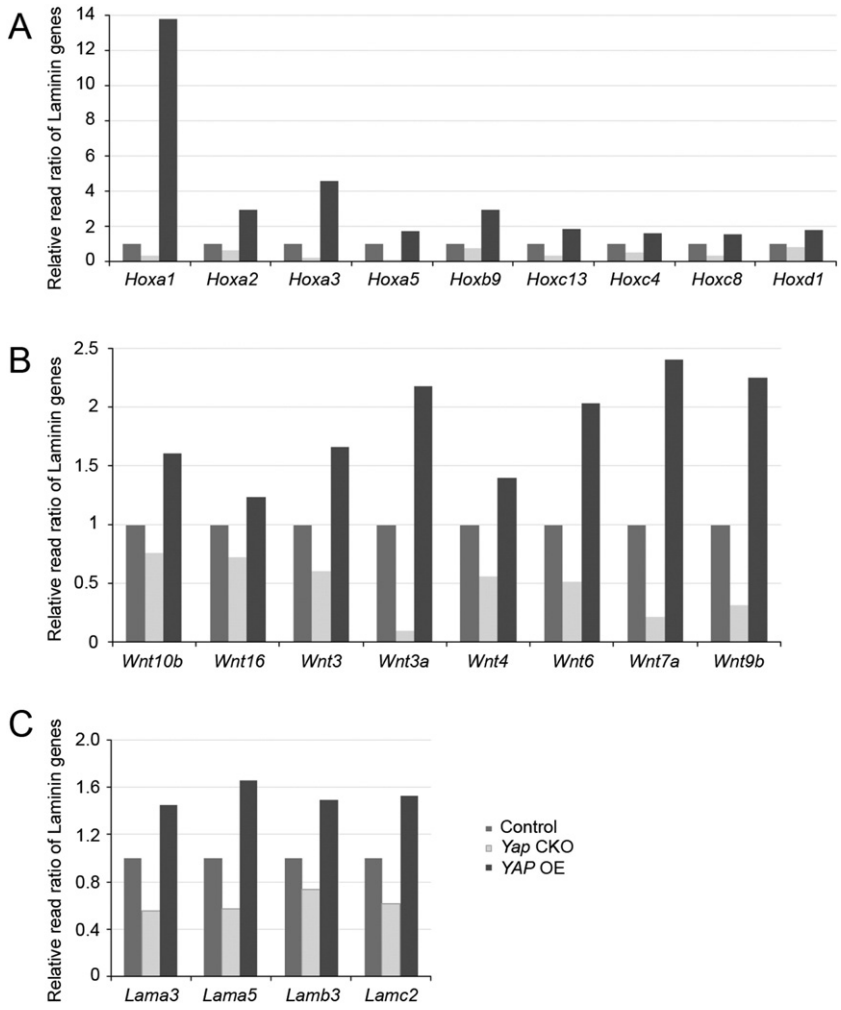

Fig. 3. The members of three gene families having concurrent transcript changes with YAP transcripts showed from the RNA-Seq data. (A) The nine members of Hox gene family showing concurrent transcript changes. (B) The eight members of Wnt gene family showing concurrent transcript changes. (C) The four members of Laminin gene family showing concurrent transcript changes.

protein gene family members. Further investigation is required to understand the regulation of their expression by YAP and the relationships among these gene families.

Acknowledgments

We thank Fernando Camargo (Boston Children's Hospital) for kindly providing the *YAP* transgenic and *Yap* CKO mice. The HSDM Dean's Scholar Award supported this investigation. The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

References

[1] M. Liu, S. Zhao, Q. Lin, X.P. Wang, YAP regulates the expression of Hoxa1 and Hoxc13 in mouse and human oral and skin epithelial tissues. Mol. Cell. Biol. 35 (8) (2015) 1449–1461.

[2] K. Schlegelmilch, M. Mohseni, O. Kirak, J. Pruszak, J.R. Rodriguez, D. Zhou, et al., Yap1 acts downstream of alpha-catenin to control epidermal proliferation. Cell 144 (5) (2011) 782–795.

[3] F.D. Camargo, S. Gokhale, J.B. Johnnidis, D. Fu, G.W. Bell, R. Jaenisch, et al., YAP1 increases organ size and expands undifferentiated progenitor cells. Curr. Biol. 17 (23) (2007) 2054–2060.

[4] H. Nguyen, M. Rendl, E. Fuchs, Tcf3 governs stem cell features and represses cell fate determination in skin. Cell 127 (1) (2006) 171–183.

[5] M. Liu, S. Zhao, X.P. Wang, YAP overexpression affects tooth morphogenesis and enamel knot patterning. J. Dent. Res. 93 (5) (2014) 469–474.

[6] L. Azzolin, T. Panciera, S. Soligo, E. Enzo, S. Bicciato, S. Dupont, et al., YAP/TAZ incorporation in the beta-catenin destruction complex orchestrates the Wnt response. Cell 158 (1) (2014) 157–170.

[7] W.M. Konsavage Jr., S.L. Kyler, S.A. Rennoll, G. Jin, G.S. Yochum, Wnt/beta-catenin signaling regulates Yes-associated protein (YAP) gene expression in colorectal carcinoma cells. J. Biol. Chem. 287 (15) (2012) 11730–11739.