DOI 10.18699/BioGenEvo-2018-28

Analysis of transcription binding and developmental genes regulated by Zic3 factor in zebrafish

Y.L. Orlov[1,2,3]*, C.L. Winata[1], I. Kondrychyn[1], S.S. Kovalev[2], A.V. Tsukanov[2]
[1] *Genome Institute of Singapore, Singapore*
[2] *Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia*
[3] *A.O. Kovalevsky Institute of Marine Biology Research RAS, Sevastopol, Russia*
** e-mail: orlov@bionet.nsc.ru*

Key words: genomics, bacteria, microbiology, sequencing, environments, GC content, bioinformatics

Motivation and Aim: Zebrafish *(D.rerio)* is a model organism for neurobiology with growing number of genome sequencing experiments. We aimed analysis of transcription regulation in development based on ChIP-seq and RNA-seq experiments [1]. Object of the study Zic3 belongs to a family of transcription factors known for their role in early embryonic patterning. In the vertebrates, loss of Zic3 function is known to disrupt gastrulation, left-right patterning, and neurogenesis. Zic genes are the vertebrate homologues of the Drosophila odd-paired gene, which is involved in early embryonic patterning. However, molecular events downstream of this transcription factor were poorly characterized as well as transcription factor binding in the genome.
Methods and Algorithms: Here we use the zebrafish as a model to study the developmental role of Zic3 in vivo. Sequencing of the 8 hpf (hours post fertilization) ChIP sample generated and the 24 hpf ChIP sample generated about 20 mln reads, about 51% of which were mappable. Genomic regions of significant enrichment representing Zic3-binding sites (peaks) were identified using the peak-calling algorithm QuEST.
Results and conclusion: Using a combination of two genomics approaches – ChIP-seq and microarray, we identified Zic3 targets, which include genes from the Nodal and Wnt pathways, and uncovered a previously unrecognized link between Zic3 and the non-canonical Wnt pathway in gastrulation and left-right patterning. Only a minority of Zic3 binding sites were found within promoter regions. We show for the first time cis-regulation of several of these target genes by Zic3. Binding site analysis of Zic3 revealed a biased distribution towards distal intergenic regions, indicative of a long distance regulatory mechanism; some of these binding sites were highly conserved during evolution and were functional enhancers. Our study establishes the zebrafish as an excellent model for genome-wide study of a transcription factor in vivo.
Acknowledgements: The research has been supported by the Ministry of Education and Science of the Russian Federation grant No. 14.W03.31.0015.

References

1. Winata C.L., Kondrychyn I., Kumar V., Srinivasan K.G., Orlov Y., Ravishankar A., Prabhakar S., Stanton L.W., Korzh V., Mathavan S. (2013) Genome-wide analysis reveals Zic3 interaction with distal regulatory elements of stage specific developmental genes in zebrafish. PLoS Genetics, 9(10): e1003852.