

A comprehensive TE-Gene network to reveal the impact of transposable elements (TEs) on physiological and pathological states

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Abstract

Transposable elements (TEs) are mobile DNA sequences that constitute the largest portion of the human genome, have been known to influence genome structures and regulate gene expression, which in turn can alter phenotypes. Given the fact that TEs are involved in the regulation of gene expression, TE-gene co-expressed relationships could predict many functional mechanisms that are not detected by analyzing only gene expression profiles. Despite the increasing amount of transcriptomic data, the functional impact of regulatory activities encoded by TEs has largely remained unexplored. Therefore, taking large RNA-seq datasets as working material, I used Spearman rank correlation, Mutual Information and Multiple regression to unveil regulatory networks linking genes and TEs in physiological and pathological states. In order to link perturbations of these networks with specific diseases, e.g. cancer, these data will be integrated within a framework of phenotypic analyses including prognosis and response to treatment. This work aims to 1) uncover the expression diversity of TE-gene networks across tissues leading to identification of tissue-specific networks, 2) shed light on TE-gene networks emerging in pathological conditions such as cancer, which may facilitate the development of targeted therapeutic strategies.

Keywords: *Transposable element, Gene regulatory network, Tissue-specificity, Disease network, Genotype-Phenotype association, Drug-Target association*

References

- [1] M. Friedli and D. Trono, The developmental control of transposable elements and the evolution of higher species, *Annu Rev Cell Dev Biol.* 2015, 31:429-51
- [2] Ecco, G., Cassano, M., Kauzlaric, A., Duc, J., Coluccio, A., Offner, S., Imbeault, M., Rowe, H. Transposable Elements and Their KRAB-ZFP Controllers Regulate Gene Expression in Adult Tissues. *Dev Cell.* 2016 Mar 21;36(6):611-23. doi: 10.1016/j.devcel.2016.02.024
- [3] M., Turelli, P. and Trono, D, Transposable elements and their KRAB-ZFP controllers regulate gene expression in adult tissues. *Dev. Cell* 36, 2016, 611-623. doi:10.1016/j.devcel.2016.02.024
- [4] Marbach, Daniel et al, Tissue-specific regulatory circuits reveal variable modular perturbations across complex diseases. *Nature methods* vol. 13,4, 2016, 366-70
- [5] Günter Schneider, Marc Schmidt-Supprian, Roland Rad & Dieter Saur. Tissue-specific tumorigenesis: context matters. *Nature Reviews Cancer* volume 17, 2017, pages 239–253
- [6] Vaquerizas J.M., Kummerfeld S.K., Teichmann S.A., Luscombe N.M.: A census of human transcription factors: function, expression and evolution. *Nature Reviews Genetics* 10(4), 2019, 252–263, doi: 10.1038/nrg2538
- [7] Chen Y., Zhu J., Lum P.Y., Yang X., Pinto S., MacNeil D.J., Zhang C., Lamb J., Edwards S., Sieberts S. K., et al.: Variations in DNA elucidate molecular networks that cause disease. *Nature* 452 (7186), 2008, 429–435, doi: 10.1038/nature06757
- [8] Pierson E, Koller D, Battle A, Mostafavi S, the GTEx Consortium. Sharing and Specificity of Co-expression Networks across 35 Human Tissues. *PLoS Comput Biol.* 2015, 11:e1004220

Biography

I majored in Bioinformatics based on Computer Science during my Master's course at Yonsei University. After graduation, I worked at Drug Discovery Department, LG Chem for over 4 years. And I am a PhD student in Laboratory of Virology and Genetics (LVG), supervised by Prof. Didier Trono at EPFL. During my PhD, I focus on how TEs activity affects gene expression and causes tissue-specific function or disease state transition in

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