Using networks to understand tissue-specific gene regulation

October 27 2017

Researchers at Brigham and Women's Hospital have discerned that different tissue functions arise from a core biological machinery that is largely shared across tissues, rather than from their own individual regulators. In a paper published in *Cell Reports*, Kimberly Glass, PhD, of the Channing Division of Network Medicine, and her team explain how they have used PANDA (Passing Attributes between Networks for Data Assimilation) to create network models of the interactions between transcription factors and genes, finding that the presence of different tissue functions is the result of subtle, tissue-specific shifts in a regulatory network. For each of these tissue-specific functions, the network has the same core components, but they're combined in different ways with added genetic and environmental information. The team analyzed data from the Genotype-Tissue Expression (GTEx) consortium, among other regulatory information sources, to reconstruct and characterize regulatory networks for 38 tissues.

PANDA, a model created by Glass and her team in 2013, was uniquely qualified for this investigation because it can more accurately model interactions between transcription factors - which help control where, when and to what extent genes get activated - and their targets. Summarizing the complex interactions between transcription factors and genes is an important step in understanding patterns in the network that inform how gene regulation gives rise to a variety of specific tissue functions.

The authors also observed that the regulation of specific tissue function

is largely independent of transcription factor expression. They note that there are approximately 30,000 genes in the human genome, but fewer than 2,000 of them encode transcription factors.

"A large number of processes must be carried out for a tissue to function properly," said Glass. "Rather than activating particular transcription factors to carry out these various processes, we find that that the networks connecting these regulators to their target genes is reconfigured to more effectively coordinate the activation of those tissue functions."

The team notes that their work highlights the importance of considering the context of specific tissues when developing drug therapies. Given that shifted regulatory networks govern different functions, this will be important in order to understand the potential side effects of drugs outside of the target tissue.

More information: Abhijeet Rajendra Sonawane et al, Understanding Tissue-Specific Gene Regulation, *Cell Reports* (2017). DOI: 10.1016/j.celrep.2017.10.001

Provided by Brigham and Women's Hospital