From milliseconds to lifetimes: dynamic behavior of transcription factors in gene networks

When living organisms are exposed to a sudden change in the environment, many genes are turned on in an organized manner to enable the organism to cope and respond to the changing environment. This coordinated genome-wide response can be abstracted as a gene network, where a few master genes regulate other genes in the network. Master regulators are usually transcription factors that can physically bind to their target genes to regulate their activity (*e.g.* “on”, “off” or fine-tuning). Therefore, understanding how transcription factors coordinate rapid and dynamic responses to environmental change, will help us understand how living organisms respond to the external environment, a topic with great relevance to health, agriculture and environmental conservation.

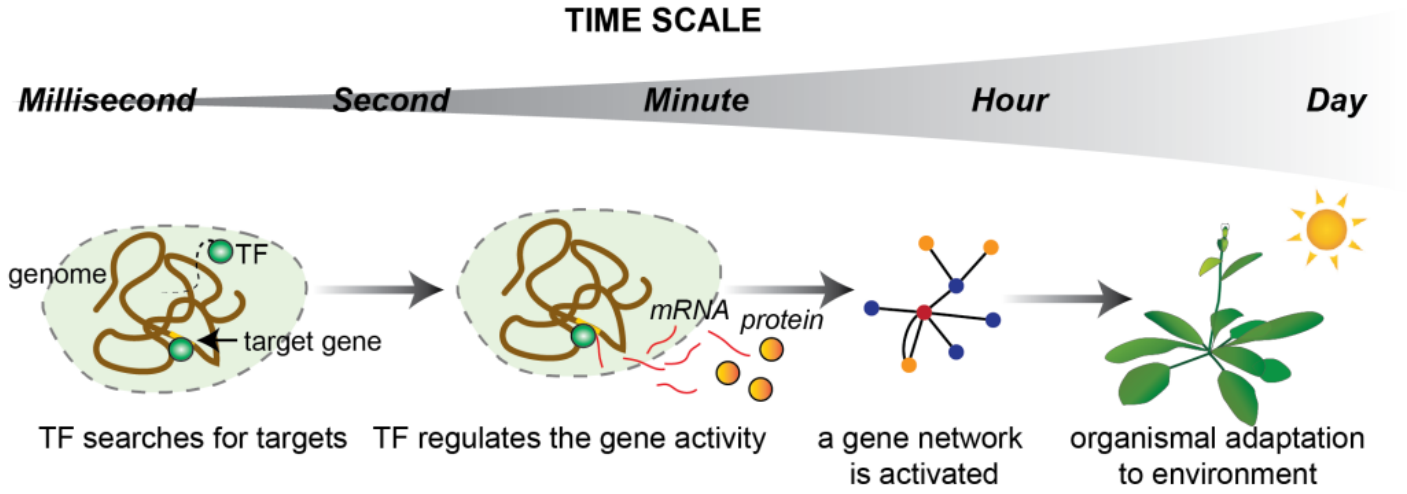

Fig.1.

Our article (Li et al., 2015, *Trends in Genetics*) addresses the dynamics of transcription factor function, which is an important, yet overlooked perspective of the function of transcription factors. In our article, we summarized recent studies on transcription factors that have considered *time* as a factor. The time scales discussed range from milliseconds to days. Collectively, we learned that transcription factors bind to their target genes in a highly dynamic manner, which leads to temporal changes of gene network activity in response to environmental stimulus (Fig. 1.). To explain how this dynamic control of gene activity is achieved, we discussed a few proposed working models,

including the “hit-and-run” transcription model for which our lab has uncovered genome-wide evidence.

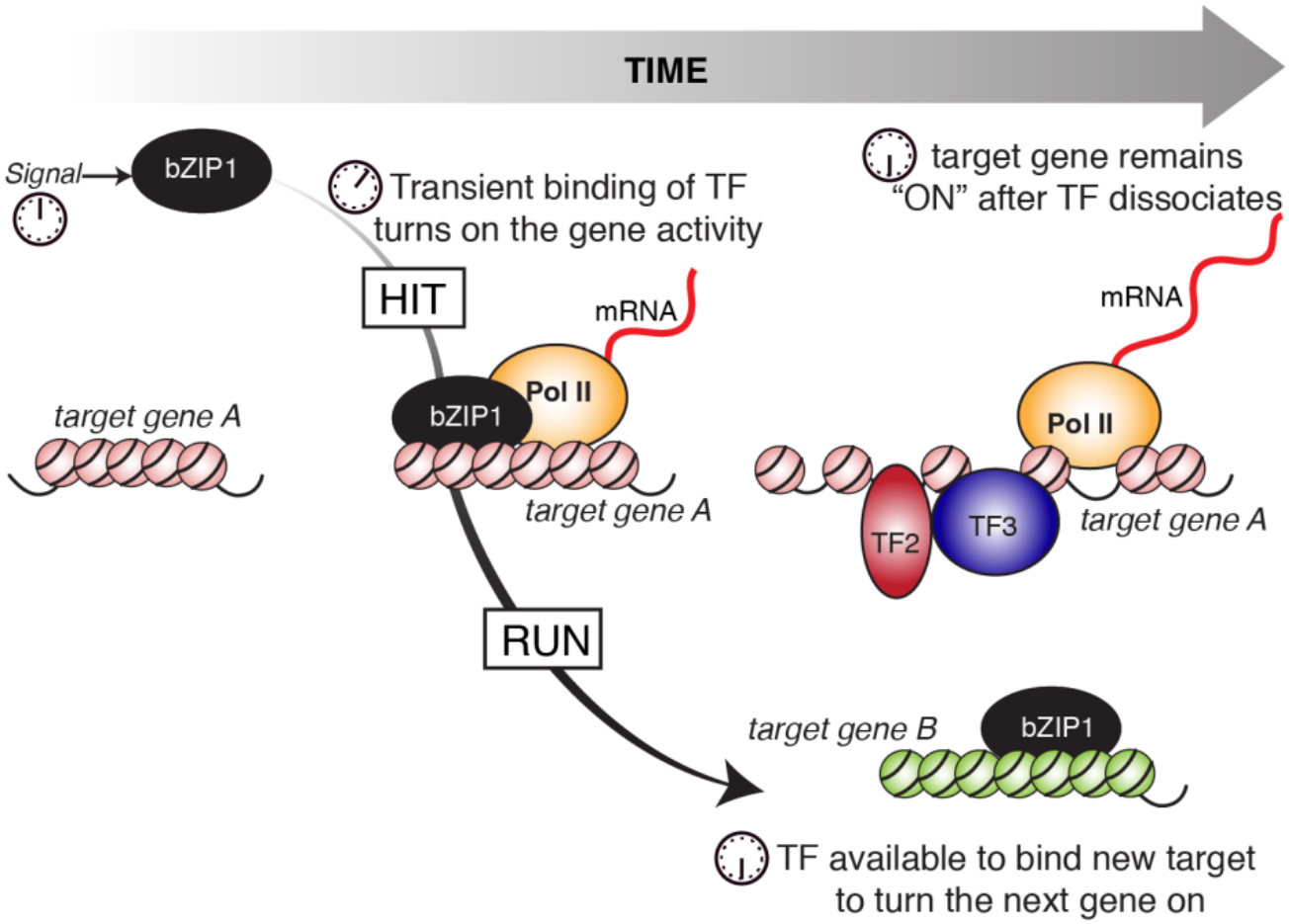

Fig.2.

In the Hit-and-Run transcription model, a master transcription factor bZIP1 binds transiently to its target gene (e.g. within 1-5 minutes of nuclear entry). This first step is known as the “Hit”. The “Hit” activates transcription of a target gene, which continues even after the TF is no longer bound to the target (the “Run”) (Fig. 2.). Interestingly, the “Hit” gene stays on, even after bZIP1 has “Run” away, possibly because bZIP1 has recruited some “buddy” transcription factors to help. We analogize this “Hit-and-Run” mechanism to Mark Twain’s Tom Sawyer’s trickery in convincing others that it is a privilege to join him to paint Aunt Polly’s fence and then sneaks away, leaving his friends to finish the job he started. It is hypothesized that this “Hit-and-Run” mechanism of bZIP1 allows it to activate a large number of genes within a short time frame. Overall, the “Hit-and-Run” model might suggest a general mechanism that allows an organism to activate a gene network

rapidly in response to an environmental signal.

Publication

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Li Y, Varala K, Coruzzi GM.
Trends Genet. 2015 Sep