Biologists capture fleeting interactions between regulatory proteins and their genome-wide targets

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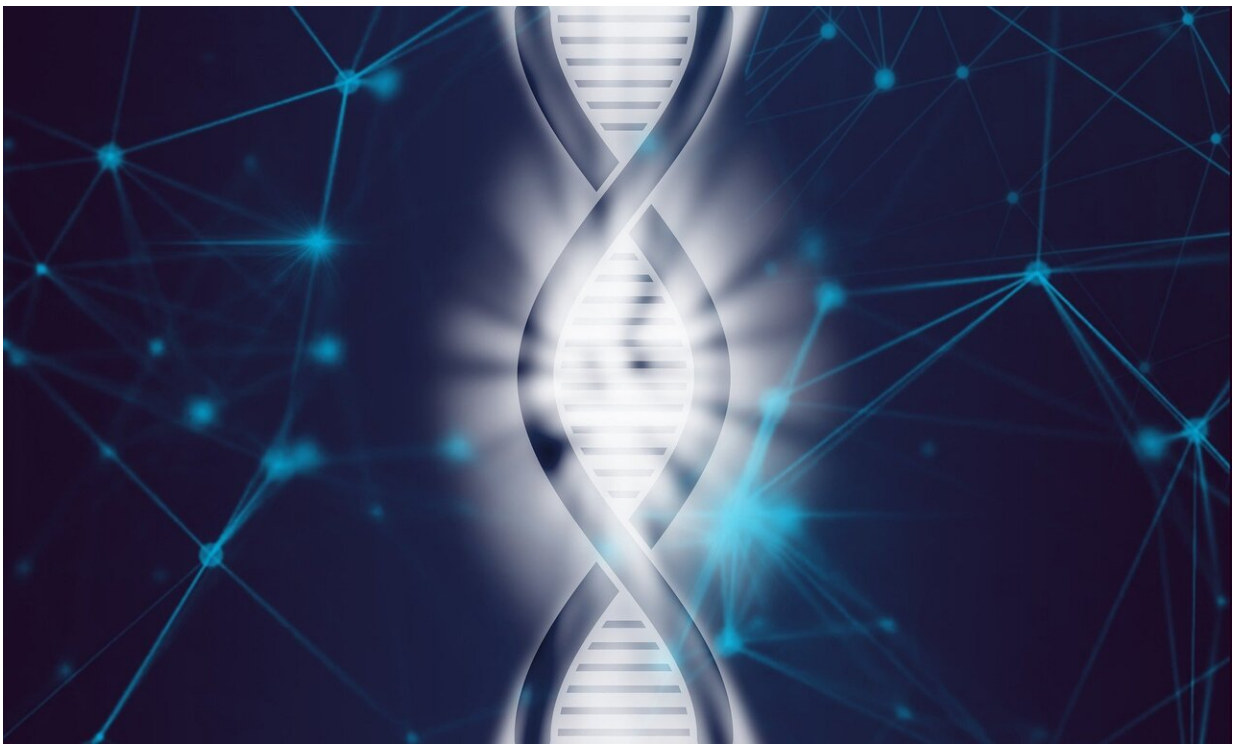

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New York University biologists captured highly transient interactions between transcription factors—proteins that control gene expression—and target genes in the genome and showed that these

typically missed interactions have important practical implications. In a new study published in *Nature Communications*, the researchers developed a method to capture transient interactions of NLP7, a master transcription factor involved in nitrogen use in plants, revealing that the majority of a plant's response to nitrogen is controlled by these short-lived regulatory interactions.

"Our approaches to capturing transient transcription factor-target interactions genome-wide can be applied to validate dynamic interactions of transcription factors for any pathway of interest in agriculture or medicine," said Gloria Coruzzi, Carroll & Milton Petrie Professor in NYU's Department of Biology and Center for Genomics and Systems Biology and the paper's senior author.

Dynamic interactions between regulatory proteins and DNA are important for triggering controlled expression of genes into RNA in response to a changing cellular or external environment. However, the underlying transient interactions between transcription factors and their genome-wide targets have been largely missed, as current biochemical methods require stable—not fleeting—interactions between a transcription factor and its DNA target.

In the *Nature Communications* study, the researchers witnessed these elusive transient interactions between NLP7, a master transcription factor in plants that regulates genes involved in nitrogen uptake for plant growth, and its target genes. Nitrogen is a key nutrient for plant development and is found in soil and fertilizer.

The researchers captured highly transient interactions of NLP7 with genome-wide targets that even defied capture by biochemical detection methods performed within minutes of NLP7 nuclear import. They did this by fusing NLP7 to a DNA methylation enzyme from bacteria, which they then induced to enter the nucleus of a plant cell. At any time NLP7

touched a gene—even briefly—it would leave a permanent methylation mark on the DNA. They also showed that this highly transient interaction between NLP7 and its target genes in the genome led to new and continued transcription of the gene into RNA.

"We found that more than 50 percent of the genes regulated by NLP7 in whole plants involve highly transient transcription factor-DNA interactions that occur within five minutes of controlled NLP7 nuclear import captured in isolated plant cells. Moreover, the transient NLP7 binding activates a transcriptional cascade that regulates more than 50 percent of the nitrogen responsive genes in whole plant roots," explained Coruzzi.

Given that more than half of gene responses to nitrogen in plants are controlled by transient interactions with NLP7, the researchers note that the discovery of these elusive genome-wide targets of NLP7 have implications for improving nitrogen use efficiency, which can benefit agriculture and sustainability.

More information: José M. Alvarez et al, Transient genome-wide interactions of the master transcription factor NLP7 initiate a rapid nitrogen-response cascade, *Nature Communications* (2020). DOI: 10.1038/s41467-020-14979-6

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