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Early-stage gene transcription creates access to DNA

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A gene contained in laboratory yeast has helped an international team of researchers uncover new findings about the process by which protein molecules bind to control sequences in genes in order to initiate gene expression, according to findings reported in the journal *Nature*.

Previously thought to be inert carriers of the genetic instructions from DNA, so-called non-coding RNAs turn out to reveal a novel mechanism for creating access to DNA required by transcriptional activation proteins for successful gene expression, according to Boston College Biology Professor Charles Hoffman, a co-author of the study with researchers from two Japanese universities.

The team focused on transcription, the first step in gene expression, whereby the blueprint of a cell's DNA is first communicated and paves the way for RNA to deliver their specific pieces of protein-synthesizing genetic coding – essentially flicking the switch that activates the gene.

Hoffman and his colleagues examined how the yeast cell senses its cellular environment and makes decisions about whether or not to express a gene, in this case fbp1, which encodes an enzyme. What they found was a preliminary transcription phase with a flurry of switches flicked "on" and then "off" as seen by the synthesis of non-coding RNA before the final "on" switch is tripped.

The non-coding RNAs initiate over one thousand base pairs of nucleotides along the DNA away from the known start site for this gene.

The group discovered that the process of transcribing non-coding RNAs is required for the eventual production of the protein-encoding RNA. The transient synthesis of these non-coding RNAs serves to unfurl the tightly wound DNA, essentially loosening the structure to allow for gene expression.

"This is a novel identification of one of the many ways gene expression can be regulated," said Hoffman. "It's a surprising discovery of why there are all these RNA molecules being made in cells that are not protein-encoding molecules. It is in fact the process of making these molecules that leads to the protein-encoding RNAs."

The paper was co-authored by Hoffman and RIKEN Advanced Science Institute scientists Kouji Hirota, Kazuto Kugou, Takehiko Shibata, Kunihiro Ohta and their colleague Tomoichiro Miyoshi at the University of Tokyo.

"I hope this leads others to find similar events occurring on other genes," said Hoffman. "A big part of this kind of work is understanding that there are other potential mechanisms for gene expression."

Source: Boston College