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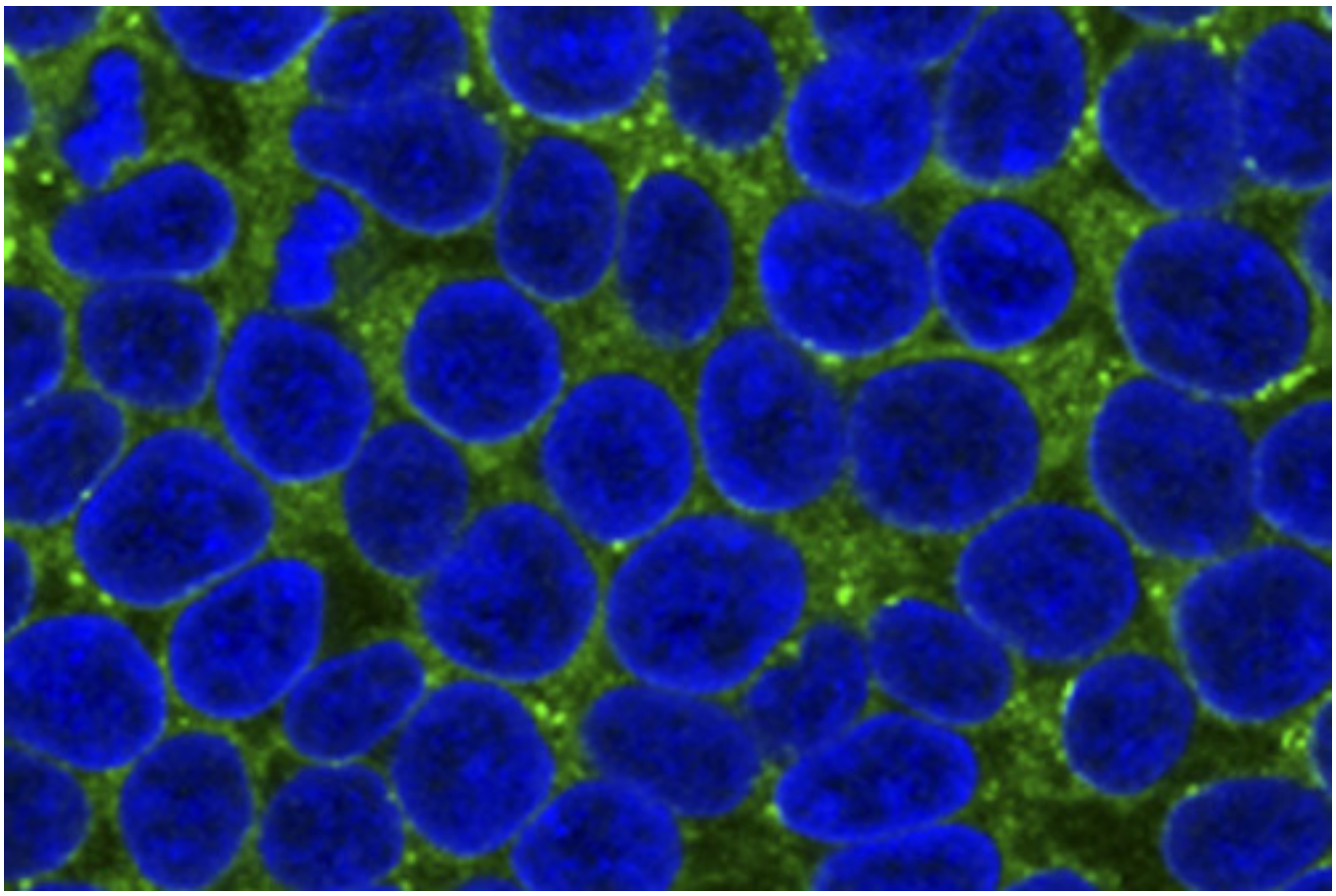

JUST THE FAQS: RNA-Binding Proteins in Stem Cells

Gene Yeo, PhD, associate professor of cellular and molecular medicine at University of California, San Diego School of Medicine, and his research group study proteins in cells that specifically bind RNA—a type of genetic material similar to DNA. Here, JUST THE FAQs breaks down their latest studies, published March 28, 2016 in *Nature Methods* and April 7, 2016 in *Cell Report*s.

What are RNA-binding proteins?

RNAs have many jobs in a cell, most notably delivering protein-building instructions from the genome to the cytoplasm. As their name suggests, RNA-binding proteins affix themselves to strands of RNA. Cells employ these proteins to keep tight control over which genes get made into proteins and which don't. RNA-binding proteins do this by stabilizing RNA, controlling where RNA is localized in a cell, and how it gets translated into proteins.

Why is it important to study RNA-binding proteins?

Not only is it important to study RNA-binding proteins in order to fully appreciate cell function and human development, RNA-binding protein malfunction can lead to diseases, such as neurodegeneration, auto-immune defects and cancer. One particular group of RNA-binding proteins — the IMP/IGF2BP family — is known to play a variety of roles in both embryonic development and cancer. But to better understand how IMP and other RNA-binding proteins work and how they can contribute to disease, researchers need to first

understand the basics: where, how and when these proteins bind RNA.

How do researchers identify *where* RNA-binding proteins bind RNA?

In their latest study, Yeo's team developed a new technique called eCLIP to study RNA-binding proteins. eCLIP combines and improves upon two recently developed laboratory methods: UV crosslinking and immunoprecipitation (CLIP) — which pulls RNA-binding proteins and their associated RNA out of cells — followed by high-throughput sequencing of that RNA.

What did the researchers find?

"Identifying RNA binding protein targets has been challenging in large scale. With eCLIP, we were able to profile 73 RNA binding proteins in two cell lines, creating an extensive resource for the RNA community," said Eric Van Nostrand, PhD, a postdoctoral researcher in Yeo's lab and first author of the Nature Methods study.

The researchers found that eCLIP improved the ability to identify true binding sites above common false positive signals, and significantly decreased the cost and failure rate of these experiments.

In a parallel effort published in Cell Reports, the researchers then used the improved efficiency of eCLIP to consider the IMP family of RNA-binding proteins. "In this study, we used genomics approaches to identify binding preferences for IMP1 and IMP2 in human stem cells," said co-first author of the IMP study Anne Conway, PhD, who was a graduate student in Yeo's lab at the time she conducted this research.

When the researchers removed IMP1 from human stem cells in the lab, the cells were less able to survive and adhere to each other. This previously unknown role of IMP1 in stem cells, and the pieces of RNA it binds, provides are new clues to aid the understanding of human development and tumor formation.

"Our study also provides a resource for other researchers interested in studying additional direct targets and functions of the IMP/IGF2BP proteins," said Van Nostrand.

Pictured: IMP1 protein regulates RNA processing in the cytoplasm of cells.

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