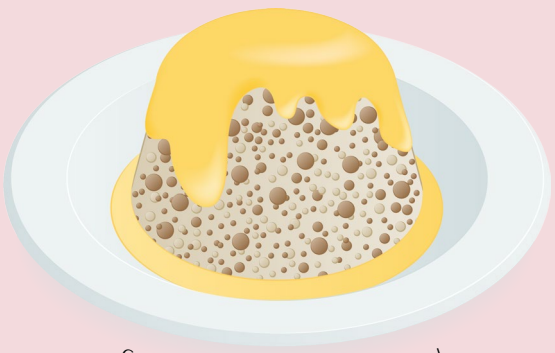
infections (West Nile virus was not investigated); *RIOK3* might, therefore, have roles in infection beyond innate immunity. Further, siRNA depletion experiments indicated that other m^{6}A-altered transcripts also influence viral infection outcomes.

Although it is still unclear precisely how all the altered m^{6}A modifications affect mRNA fate, viral modulation of m^{6}A levels could involve a sequence-targeting mechanism or the m^{6}A reading and/or writing machineries. Virus-induced changes in m^{6}A levels occur in nascent RNA, suggesting that m^{6}A is added during transcription and does not change thereafter. Thus, m^{6}A regulation of RNA metabolism leads to rapid, tuneable changes in the abundance of specific mRNAs and proteins during viral infection.

Caroline Barranco

ORIGINAL ARTICLE Gokhale, N. S. et al. Altered m^{6}A modification of specific cellular transcripts affects *Flaviviridae* infection. *Mol. Cell* https://doi.org/10.1016/j.molcel.2019.11.007 (2019)
RELATED ARTICLE Zaccara, S. et al. Reading, writing and erasing mRNA methylation. *Nat. Rev. Mol. Cell Biol.* **20**, 608–624 (2019)



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and increased accumulation of nascent transcripts.

In summary, the study indicates that nuclear speckles have a 'gene expression amplification' function. Further studies will be required to elucidate the mechanism of gene regulation by nuclear-speckle association.

Minju Ha, Associate Editor,
Nature Communications

ORIGINAL ARTICLE Kim, J. Gene expression amplification by nuclear speckle association. *J. Cell Biol.* https://doi.org/10.1083/jcb.201904046 (2019)

Journal Club

RISE OF THE NEGLECTED REPEATS RNA

In 2014, Jeanne Lawrence and her colleagues published a very beautiful and convincing microscopy study describing the identification of a class of 'chromosomal RNAs' with several unusual properties. I often recommend this article to newcomers in my laboratory, to demonstrate how microscopy can be employed to circumvent the limitations of other techniques and provide important and surprising findings.

The authors discovered that a class of RNA consisting mainly of long interspersed nuclear element 1 (LINE1) repeats, is present at very high levels in cell nuclei (being even more abundant than ribosomal RNA), a finding that was previously missed owing to the difficulty of extracting these RNAs. Indeed, the ratio of RNA to DNA obtained using RNA FISH was 4:1, whereas following extraction and qPCR it declined to less than 1:1,500. Consequently, even though these repeat elements — many of which are located in gene introns — occupy almost half of our genome, they have previously been considered 'junk' and routinely removed or overlooked in most genomic analyses.

> "this was visualized… as RNA 'holes' at compact chromatin"

The repeats RNAs were exceptionally stable — their levels remained unchanged even after 30 h of transcription inhibition — and they were localized exclusively in the vicinity of their parent chromosomes, in contrast to most other RNAs, which are less stable and leave their site of transcription. Moreover, the repeats RNAs were associated with accessible euchromatin and were excluded entirely from heterochromatin; this was visualized under the microscope as RNA 'holes' at compact chromatin.

Finally, employing both fluorescence and electron microscopy, Hall et al. demonstrated that repeats RNAs were released from chromatin during mitosis and had to be resynthesized in the daughter cells early in the G1 phase to allow reopening of chromatin. Failure in resynthesis led to widespread chromatin compaction in G1 and to the compacted chromatin having unusual shapes, including spindle-like protrusions.

In addition to visualizing the life cycle of these abundant and important repeats RNAs in association with chromatin, this study helped me understand our own unexpected discovery that histones and chromatin precipitate when RNA is removed. I realized that, particularly in light of RNA abundance in chromatin, the negative charge of RNA might influence the local ionic environment. This insight led to our recent discovery that LINE1 RNAs bind to histones and can open compacted chromatin by inhibiting electrostatic interactions between histones and DNA.

This brief history underscores the power of microscopy, not only in the sense that seeing is often prerequisite to believing, but also by providing insight into the previously underappreciated repeat sequences.

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