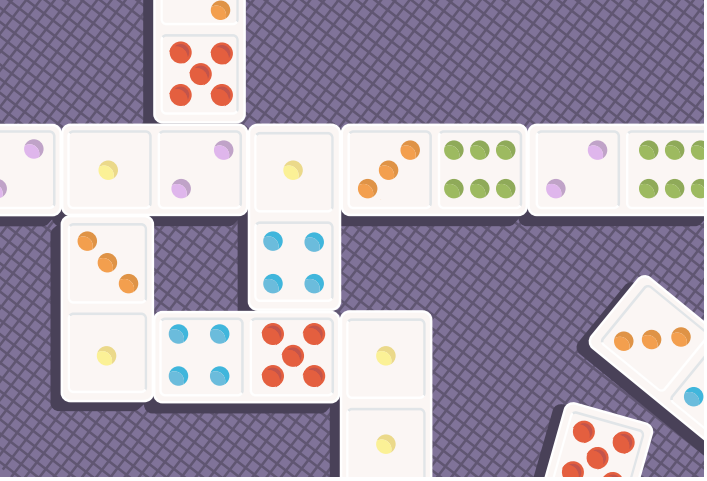

Credit: Caio Bracey/ Springer Nature Limited

motifs can result in protein mistrafficking and may be a direct cause of pathology.

In summary, this study demonstrates the direct role of mutations in IDRs in modulating protein–protein interactions and provides a first glimpse into how such mutations could contribute to disease. In the future, it will be interesting to systematically survey different mutations found in IDRs and investigate their impact on the IDR interactome.

Paulina Strzyz

ORIGINAL ARTICLE Meyer, K. et al. Mutations in disordered regions can cause disease by creating dileucine motifs. *Cell* https://doi.org/10.1016/j.cell.2018.08.019 (2018)

> “ATR activity decreases when cells progress from S phase to G2 … permitting FOXM1 activation and cell cycle progression”

Whereas RAD9 and TOPB1 deletion had little effect on ATR in S phase, silencing of ETAA1 reduced ATR activity in S phase cells.

With the knowledge that the S/G2 transition is governed by ATR, the next question to answer will be how ATR senses the completion of replication to enable this transition. The authors propose an attractive model in which ETAA1 is recruited by RPA to nascent ssDNA during replication to keep ATR in an activated state until replication is completed.

These findings may have broader implications in human disease as overexpression of FOXM1 is found in human cancers. Given the role of FOXM1 in cell cycle progression, this provides a potential mechanistic explanation for the genomic instability found in various malignancies.

Michelle Trenkmann, Associate Editor, Nature Communications

ORIGINAL ARTICLE Saldivar, J. C. et al. An intrinsic S/G_2 checkpoint enforced by ATR. *Science* **361**, 806–810 (2018)
FURTHER READING Saldivar, J. C. et al. The essential kinase ATR: ensuring faithful duplication of a challenging genome. *Nat. Rev. Mol. Cell Biol.* **18**, 622–636 (2017)

In the news

HATS OFF FOR THE LASKER AWARDEES

With the announcement of the Lasker Awards, September is an exciting month for molecular biology. This year, the Albert Lasker Basic Medical Research Award honours C. David Allis (Rockefeller University, USA) and Michael Grunstein (UCLA, USA) for their work that laid the ground for understanding the key roles of histone post-translational modifications (PTMs) in gene regulation.

Pioneering studies in the 1970s attributed histones with the important yet seemingly dull function of packaging DNA into chromatin. This function as ‘packing material’ left histones underappreciated until the 1990s, when it was largely accepted that histones serve as key regulators of gene expression. Our current understanding of the role of histones in the regulation of chromatin function has been greatly influenced by the curious minds of Grunstein and Allis.

Grunstein pioneered the work on histones in yeast. Throughout the 1980s and early 1990s he took advantage of emerging genomic techniques to probe the role of individual histones and their sequence on yeast physiology. Grunstein advocated that histones are more than DNA packing material and that they have an active part in transcription regulation. He was particularly interested in histone amino-terminal tails, which were known by that time to undergo PTMs. Although the links between PTMs at histone tails and gene expression were postulated by Vincent Allfrey as early as 1964, it was not until 1996 that direct evidence for such a link was provided by the Allis lab.

Upon starting his lab in 1981, Allis embarked on a search for a protein with histone acetyltransferase (HAT) activity in the single-celled protozoan *Tetrahymena thermophila*. This endeavour proved to be tedious, but the effort paid off, culminating in the identification of a homologue of the yeast transcription co-activator Gcn5 as a HAT. This discovery provided a starting point for functional studies of the histone PTMs, leading to current applications of the accumulating knowledge of the histone PTM code in biomedicine. In reference to this progress in the video produced by the Lasker Foundation, Allis said “And there’s just clear examples of disease. Mistakes made in setting this [histone PTM code] up seem to be very clearly causing cancer. Now, even if you didn’t find it just academically interesting, it is medically interesting.”

The 2018 Lasker–Koshland Special Achievement Award in Medical Science has also been awarded to a molecular biologist, Joan Argetsinger Steitz (Yale University, USA) in honour of four decades of her continued leadership in biomedical science. Steitz is best known for her ground-breaking work leading to the identification of small nuclear ribonucleoproteins (snRNPs) and the description of their roles in mRNA splicing. But Steitz’s career goes beyond scientific achievements: she has been a strong advocate for the position of women in science as well as a model mentor for young scientists. As described by Manuel Ares, Jr (University of California, Santa Cruz, USA) “She has just been so good at every part of this enterprise that we call being a scientist” (source: video by Lasker Foundation). This description summarizes to the point the decision of the Lasker Award committee to acknowledge Steitz’s remarkable contributions to shaping modern science.

Paulina Strzyz

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