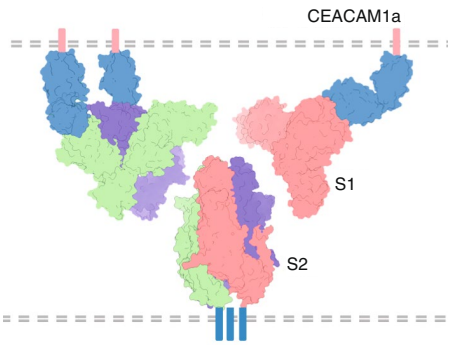
HOST-PATHOGEN INTERACTIONS

Viewing spikes

PLoS Pathog. **16**, e1008392 (2020)



Credit: PLoS

Coronaviruses are characterized by their envelope-anchored spike proteins that, through binding to a host receptor, facilitate membrane fusion and entry into host cells. The spikes consist of a trimeric membrane-fusion S2 stalk with three receptor-binding S1 heads at the tips. While mouse hepatitis coronavirus (MHV) uses the N-terminal domain of its S1 (S1-NTD) to bind its host receptor, it is unclear how it can play a role in activating membrane fusion. To gain more insight into the MHV–host interaction, Shang et al. solved the cryo-EM structure of the prefusion spike with its mouse receptor CEACAM1a. This revealed that three receptors bind via the spike NTDs to the sides of the spike trimer. Although the spike protein stays in a prefusion conformation upon receptor binding, S1 does move up and away from S2, loosening the packing of the spike protein and rendering it more prone to transition to its postfusion conformation. The authors verified the structural results biochemically, with negative-stain EM, and with MHV entry assays to be associated with later membrane fusion. The structure also shows evidence of CEACAM1a bending that might facilitate dissociation of S1 from S2. These results point to structural changes associated with receptor binding that prime the virus for fusion with host cells. *MB*

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METAL HOMEOSTASIS

An iron–sulfur grip

Mol. Cell **78**, 31–41 (2020)

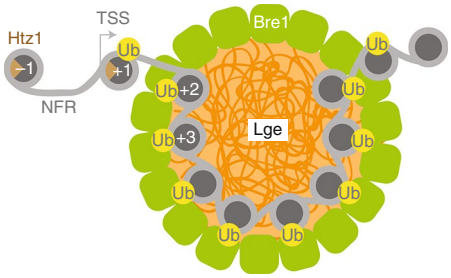
In mammalian cells, iron homeostasis is regulated through iron regulatory proteins binding to iron-responsive mRNA elements. As part of this process, F-box and leucine-rich repeat protein 5 (FBXL5) binds to and promotes the ubiquitin-mediated degradation of iron regulatory protein 2 (IRP2) when iron is plentiful. In the course of investigating how FBXL5 recognizes IRP2, Wang and Shi et al. uncovered an iron–sulfur cluster in FBXL5. Structure determination of the FBXL5–IRP2 complex by cryo-EM revealed that although the cluster is not directly at the FBXL5–IRP2 interface, it contributes to IRP2 recognition via a hydrogen bonding network involving the backbone of two of the cluster's cysteine ligands. Blocking cluster binding through mutagenesis or chemical reduction of the cluster prevented IRP2 recruitment, indicating its role as a redox switch controlling oxygen dependence for IRP2 binding. The role of this iron–sulfur cluster in regulating FBXL5–IRP2 recognition illustrates one method by which the cell senses and responds to iron and oxygen availability. *CD*

https://doi.org/10.1038/s41589-020-0536-7

POST-TRANSLATIONAL MODIFICATIONS

A reaction chamber

Nature **579**, 592–597 (2020)



Credit: Nature

Monoubiquitination of histone H2B plays important roles in nucleosome assembly and transcriptional regulation in yeast and mammals. It has been proposed that the yeast E3 ligase Bre1 installs ubiquitin on H2B in a linear manner by interacting with RNA polymerase II during transcription. Gallego et al. now characterize a new model for ubiquitination of H2B independent of RNA polymerase II. The authors found that a Bre1-interacting protein, Lge1, can form droplets via liquid–liquid phase separation (LLPS) mediated by its intrinsically disordered domain. Bre1 encases the Lge1 droplets to regulate the entry of the E2 enzyme Rad6 and nucleosomes into the droplets. Formation of LLPS and the interaction between Lge1 and Bre1 are both required for H2B ubiquitination within gene bodies. Furthermore, using protein sedimentation assays and cellular imaging, the authors showed that a large complex of Lge1 and Bre1 exists in cells. This study unveils a vital role for LLPS in organizing molecular reaction chambers to regulate the post-translational modification of chromatin. *YS*

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CHEMICAL TOOLS

Know your neighbors

Science **367**, 1091–1097 (2020)

Existing spatial proximity proteomic methods such as APEX utilize enzymes that modify amino acid residues in neighboring proteins within a cellular compartment or microenvironment. However, these approaches are not amenable to revealing short-range interactions with temporal control. Geri et al. devised a light-inducible spatial proximity system, μMap, which uses blue light to excite an iridium-based photocatalyst to enable labeling of neighboring proximal proteins within a 1–10 nm radius. Blue-light exposure excites the catalyst conjugated to an antibody, which recognizes a target of interest to activate a biotinylated diazirine probe that modifies neighboring proteins, which can be identified through LC–MS analysis. The level of biotinylation correlates with the duration of blue-light exposure. The authors performed μMapping on programmed-death ligand 1 (PD-L1) in B cells, identifying CD30 and CD300A as potential new interactors. Finally, μMapping enabled *trans*-labeling of proteins on T cells during immunosynapse formation, confirming the utility of μMapping to detect protein interactions on the cell surface with close proximity and high precision. *GM*

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