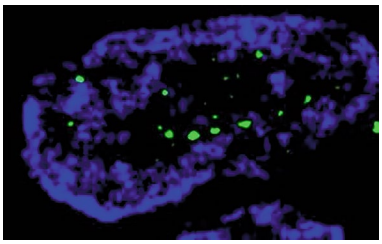
PHASE SEPARATION

Caught with the drugs

Science **368**, 1386–1392 (2020)



Credit: Alessandra Dall'Agnese

Cellular condensates are membraneless organelles that compartmentalize biomolecules. In particular, the nucleus contains a number of condensates, defined by molecular markers such as MED1 and BRD4 for transcriptional condensates, that are sufficient on their own to produce droplets. To test whether small molecules also selectively concentrate in particular condensates, Klein et. al tested the effects of fluorescently labeled cisplatin and tamoxifen on different nuclear condensates. Both compounds concentrated specifically in MED1 condensates while diffusing easily through other condensates. Analysis of a library of fluorescent compounds revealed that π–π or π–cation interactions facilitated entry into MED1 condensates by interaction with aromatic residues in MED1. Accumulation of cisplatin in MED1 condensates resulted in increased target engagement, and disruption of the MED1 condensate by BRD4 inhibition reduced the effect of cisplatin. Overall, the findings of Klein et al. will enable the rational design of small-molecule therapeutics to target specific nuclear condensates. *GM*

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HYDROGENASES

Stick-on silver

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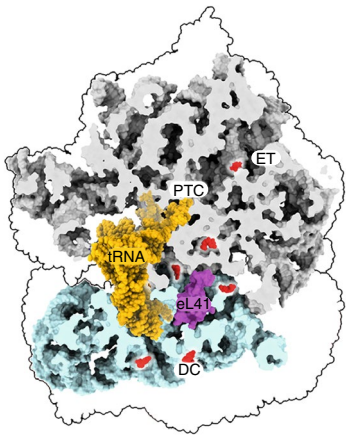
Hydrogenases are powerful biocatalysts for the production of molecular hydrogen. However, many hydrogenases either are susceptible to oxygen inactivation or, in the case of *Escherichia coli* Hyd-1, are unable to produce hydrogen because their electron-transferring Fe-S clusters are too oxidizing. To make Hyd-1 a more robust hydrogen producer, Zhang et al. chose two sites near the distal [4Fe–4S] cluster where electrons initially enter Hyd-1 and covalently attached a silver nanocluster (AgNC) to the enzyme surface to make it photoactivatable. The AgNC attached via a cysteine residue installed at either site endowed Hyd-1 with the ability to produce hydrogen at pH 6 under anaerobic or aerobic conditions upon illumination. Covalent, site-specific attachment of the AgNC was necessary for activity, as wild-type Hyd-1 incubated with free AgNC was not active. Electrochemical experiments with AgNC-Hyd-1 complexes indicated that the AgNC is able to capture energized electrons at the protein surface, shuttling them to the internal electron transfer pathway via the distal [4Fe–4S] cluster. This approach provides a potentially versatile method for engineering enzymes with increased catalytic activity in reduction reactions. *CD*

https://doi.org/10.1038/s41589-020-0605-y

RNA MODIFICATION

Hot editing sites

Nature https://doi.org/10.1038/s41586-020-2418-2 (2020)



Credit: Nature

N^4-Acetylcytidine (ac^4C) is a conserved RNA modification catalyzed in humans by the acetyltransferase NAT10. To profile RNA sites targeted by NAT10, Sas-Chen et al. developed ac^4C-seq, which uses acid-catalyzed reactivity enhancement to reduce ac^4C such that the resulting product can induce C-to-T misincorporation in reverse transcription and be read out in sequencing at single-nucleotide resolution. Using this method, the authors identified a common motif for NAT10 substrates and found that ac^4C is distributed differently in eukaryotes and archaea. Ac^4C is undetectable in eukaryotic mRNA but can be induced by overexpression of the NAT10 acetyltransferase complex. In hyperthermophilic archaea, ac^4C exhibits pervasive distribution in all types of RNAs, and its abundance increases with temperature. Knocking out the NAT10 homolog in archaea induces decreased ac^4C across all RNA types and reduced fitness at higher temperatures. Based on the structures of archaeal ribosomes, cytidine acetylation may stabilize the ribosome by replacing solvent molecules at higher temperatures. This study provides a useful tool for profiling cytidine acetylation and lays a foundation for further functional studies. *YS*

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BACTERIA-HOST INTERACTIONS

A sensory override

Nature https://doi.org/10.1038/s41586-020-2395-5 (2020)

Pathogenic bacteria can alter the olfactory behavior of the nematode *Caenorhabditis elegans*, and O'Donnell et al. have now found that commensal gut bacteria can do so as well. Among several commensal strains, the authors found that ingestion of *Providencia alcalifaciens* strains including JUb39 by the worms led to decreased avoidance of the repellant 1-octanol. Metabolomic analysis showed that *Providencia* produce tyramine, a biogenic amine involved in octanol avoidance. However, neuronally produced octopamine via a host hydroxylase enzyme, not its precursor tyramine, was found to be necessary for the JUb39-mediated decrease in octanol avoidance. Examination of *C. elegans* mutants defective for tyramine production from tyrosine and octopamine production from tyramine suggests that tyramine produced by the bacteria is converted to octopamine by the worms. The authors further showed that octopamine acts on the neuronal OCTR-1 octopamine receptor to mediate the JUb39-mediated response to octanol, and this microbe–host interaction leads to preferential selection of these bacteria by the worms. These results define a mechanism by which bacteria modulates host sensory behavior to promote the fitness of both organisms. *MB*

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