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IN BRIEF

BACTERIAL PHYSIOLOGY

Building a bacterial ribosome

Biogenesis of the mature bacterial ribosome requires the stepwise association of ~50 ribosomal proteins and intricately folded rRNA, and involves ~100 molecular chaperones. Each bacterium can generate ~100,000 ribosomes per hour, and therefore the direct visualization of ribosome biogenesis has been challenging. Davis *et al*. genetically depleted the essential bL17 large subunit (LSU) ribosomal protein in *Escherichia coli*, and they then characterized the accumulated stalled assembly intermediates using chemical probing, mass spectrometry and single-particle cryo-electron microscopy. The authors identified 13 distinct LSU intermediates that were resolved to ~4–5 Å, which revealed the arrangement of the intermediates in an assembly pathway in which blocks of structured rRNA and protein are cooperatively assembled. Assembly of mature ribosomes was shown to be flexible, with alternative assembly pathways being used when ribosomal components were limiting.

ORIGINAL ARTICLE Davis, J. H. *et al*. Modular assembly of the bacterial large ribosomal subunit. *Cell* **167**, 1610–1622.e15 (2016)

VIRAL INFECTION

Fine tuning HCV replication

Efficient replication of hepatitis C virus (HCV) in cell lines requires the acquisition of host-specific adaptive mutations; however, the molecular basis for this adaptation has remained unsolved. Harak *et al*. report that adaptive mutations in the genes encoding viral NS5A and NS5B regulate the activity of the host phosphatidylinositol 4-kinase-α (PI4Kα; a kinase that alters the lipid composition of cellular membranes by converting phosphatidylinositol to phosphatidylinositol 4-phosphate (PI4P)). In the host, HCV NS5A and NS5B proteins interact with PI4Kα to generate PI4P-rich microenvironments that are permissive for viral replication; however, increased PI4Kα levels that exist in hepatoma cell lines restrict HCV replication. The authors found that loss-of-function adaptive mutations in NS5A and NS5B prevented overactivation of PI4Kα in cell lines, which promoted the replication of wild-type isolates in cell cultures.

ORIGINAL ARTICLE Harak, C. *et al*. Tuning a cellular lipid kinase activity adapts hepatitis C virus to replication in cell culture. *Nat. Microbiol.* **2**, 16247 (2016)

PARASITE BIOLOGY

Busting out from the inside

Malaria parasites traverse through various cells within their human hosts and mosquito vectors to complete their life cycles. Although the mosquito cell traversal protein for ookinetes and sporozoites (CelTOS) is an essential protein for traversal of malaria parasites, and thus critical for the transmission and pathogenesis, its molecular role has remained elusive. To gain insight into its function, Jimah *et al*. determined the crystal structure of the CelTOS protein and found that it resembled a viral membrane fusion protein and a bacterial pore-forming toxin. They discovered that CelTOS binds to phosphatidic acid on the inner leaflet of cellular membranes and damages membranes by pore formation. This study provides important mechanistic insights into the action of the malarial CelTOS protein and indicates that CelTOS facilitates malaria plasma membrane breach and exit in infected cells. This study will also inform the development of therapeutics that target CelTOS.

ORIGINAL ARTICLE Jimah, J. R. *et al*. Malaria parasite CelTOS targets the inner leaflet of cell membranes for pore-dependent disruption. *eLife* **5**, e20621 (2016)