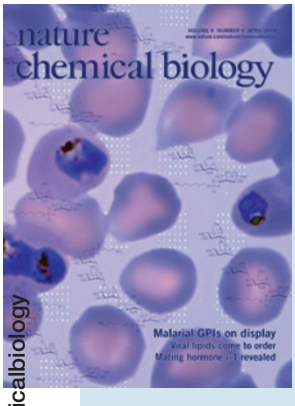


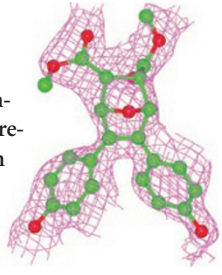
Antimalarial antibodies

Glycosylphosphatidylinositol (GPI) accounts for as much as 90% of protein glycosylation in protozoan parasites and is an important malarial toxin. Anti-GPI antibodies are found in the sera of individuals in regions with endemic malaria, and recent studies with a rodent model have suggested that GPI-based vaccines may be protective against malaria. However, the heterogeneous nature of GPIs purified from natural sources has made it difficult to correlate specific anti-GPI antibodies with antimalarial protection. Kamena *et al.* have now created a 'GPI chip' by spotting synthetic GPI glycans onto glass slides. Using this chip, the authors characterized anti-GPI antibodies from people in malaria-endemic and malaria-free regions before and after malarial exposure, demonstrating the importance of this chemical tool for defining antimalarial antibody epitopes. **[Brief Communications, p. 238; News & Views, p. 223]** *JK*

Acetyllysine encoded

Many cellular proteins have been shown to be post-translationally acetylated, and this modification is involved in regulating processes from chromatin packing to DNA repair. Despite its biological importance, understanding the functional consequences of acetylating specific protein lysines has proven challenging. Neumann *et al.* have now developed a method for site-specifically incorporating N^{ε}-acetyllysine into recombinant proteins in *Escherichia coli*. Starting from the pyrrolysyl tRNA synthetase, the authors evolved an N^{ε}-acetyllysine tRNA synthetase that was orthogonal to the *E. coli* protein translational machinery and could insert the modified amino acid at amber stop codons. This general method for encoding N^{ε}-acetyllysine–containing proteins will open up new avenues for understanding the molecular effects of acetylation. **[Brief Communications, p. 232]** *JK*

Steroid receptors on ice



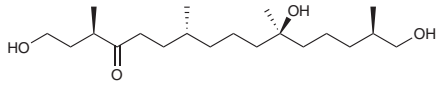
Signaling via steroid receptors is known to involve the rearrangement of several distinct portions of the protein and interaction with ancillary coactivators, but the molecular basis of receptor signaling through different downstream factors is not well understood. Nettles *et al.* now report a new technique for receptor crystallography in which single-residue mutations stabilize the receptor in known agonist- and antagonist-bound structures; cocrystallization and soaking experiments allow the generation of ten different structures of the estrogen receptor. These stabilizing mutations also facilitate the first structural determination of an apo receptor, which reveals a previously unknown channel by which ligands can access the active site. A comparative analysis of these structures demonstrates the specific molecular motions required for signaling via NF-κB. [Articles, p. 241; News & Views, p. 226] *CG*

Written by Mirella Bucci, Catherine Goodman, & Joanne Kotz

Chemical rescue of fragile X

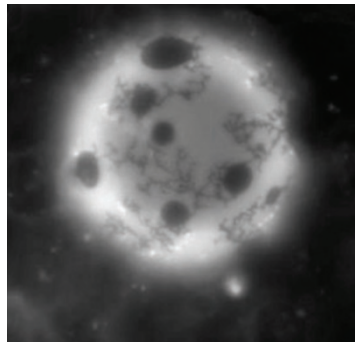
Fragile X syndrome is an inherited form of mental retardation caused by a loss of function in the fragile X mental retardation protein (FMRP), an RNA-binding protein that regulates the translation of genes involved in neurite and synapse development. The complex nature of this disease has made it difficult to develop a high-throughput assay to identify potential drug leads. Taking advantage of a *Drosophila* model system, Chang *et al.* screened 2,000 known drugs and bioactive compounds to identify small molecules that could rescue disease phenotypes. Of nine validated hits, three targeted the GABAergic pathway and two targeted the muscarinic acetylcholine receptor pathway. By characterizing the effects of these small molecules, this study provides new information about fragile X syndrome signaling pathways and suggests new therapeutic targets for the disease. **[Articles, p. 256]** *JK*

Hormone α1 takes shape



Hormone α1 was previously identified as an important molecule that causes *Phytophthora* cells to become oospores, a protective form that allows the mold to survive for long periods in adverse conditions. However, because the compound is difficult to isolate and has a complex structure that cannot be assigned by standard methods, it has not been possible to conclusively determine its structure. Yajima *et al.* now report two complimentary synthetic pathways to make several stereochemical isomers of the hormone; biological testing confirms that the *R,R,R,R* isomer is the true natural product. This insight ends a 70-year search for the compound's shape and opens the door for biological studies into and defense against the destructive *Phytophthora* fungi. [Brief Communications, p. 235] *CG*

Lipids bud in order



Although the influenza virus buds from the plasma membrane of host cells, the lipid composition of the viral membrane differs from that of the host. The viral membrane is enriched in cholesterol and glycosphingolipids, lipids that partition in the liquid ordered phase, a membrane domain that is characterized by extended hydrocarbon chains. Polozov *et al.* have used magic angle spinning NMR to characterize the motions and lateral organization of lipids within intact viral membranes. At temperatures that support viral assembly, they found lipids to be in multiple states both in intact viruses and in extracts containing lipids and proteins. This suggests that only lipids, and not proteins, contribute to membrane ordering and organization and that ordered regions, commonly referred to as lipid 'rafts', exist within the intact viral membrane. It is possible that the virus selectively buds from such host membrane micro- or nanodomains. **[Articles, p. 248; News & Views, p. 225]** *MB*