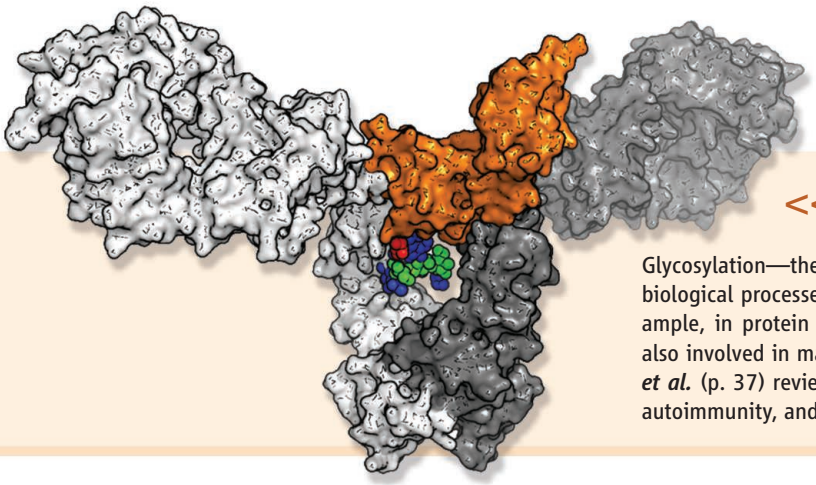


<< Understanding Glycosylation

Glycosylation—the covalent addition of carbohydrates to proteins—is central to many biological processes. Recent advances in understanding the roles of glycans—for example, in protein folding and immune regulation—have revealed that glycans are also involved in many disease conditions, from cancer to microbial infection. **Dalziel *et al.*** (p. 37) review the current knowledge of glycans in pathogen invasion, cancer, autoimmunity, and congenital diseases.

Bright Lights

Gamma-ray bursts (GRBs), bright flashes of gamma-ray light, are thought to be associated with the collapse of massive stars. GRB 130427A was detected on 27 April 2013, and it had the longest gamma-ray duration and one of the largest isotropic energy releases observed to date (see the Perspective by **Fynbo**). **Ackermann *et al.*** (p. 42, published online 21 November) report data obtained with the Fermi Gamma-Ray Space Telescope, which reveal a high-energy spectral component that cannot be accounted for by the standard external shock synchrotron radiation model. **Vestrand *et al.*** (p. 38, published online 21 November) report the detection of an extremely bright flash of visible light and unexpected similarities between the variations of optical light and the highest-energy gamma rays that indicate a common origin. A detailed analysis of the first pulse of GRB 130427A by **Preece *et al.*** (p. 51, published online 21 November) suggests that existing models cannot explain all the observed spectral and temporal behaviors simultaneously. **Maselli *et al.*** (p. 48, published online 21 November) present x-ray and optical light curves of the burst's prompt emission as well as of its afterglow as recorded by the Swift satellite and a range of ground-based telescopes.

Unadorned Aziridines

Multiple catalytic methods have been developed to make aziridines—strained triangular carbon-nitrogen-carbon rings that function as versatile synthetic intermediates. However, the majority require protection of the nitrogen precursor with a sulfonyl group that is subsequently inconvenient to remove. **Jat *et al.*** (p. 61; see the Perspective by **Türkmen and Aggarwal**) used a hydroxylamine derivative as the nitrogen source together with an established rhodium catalyst to prepare a wide range of unprotected aziridines, with nitrogen bonded simply to hydrogen or a methyl group.

CREDITS (TOP TO BOTTOM): DALZIEL *ET AL.*; KIRMANI *ET AL.*

Playing Hide and Seek

Targeted cancer therapies have shown promising results in patients, but few of these drugs provide long-term benefits because tumor cells rapidly develop drug resistance. **Nathanson *et al.*** (p. 72, published online 5 December) show that glioblastoma cells can become resistant to erlotinib, an epidermal growth factor receptor (EGFR)–targeted drug, by eliminating extrachromosomal copies of the mutant *EGFR* gene. After a period of drug withdrawal, the mutant *EGFR* gene reappears on extrachromosomal DNA and the tumor cells become resensitized. The discovery that cancer cells can evade drug therapy by this "hide and seek" mechanism may help to optimize the dosing schedule of erlotinib in glioblastoma patients.

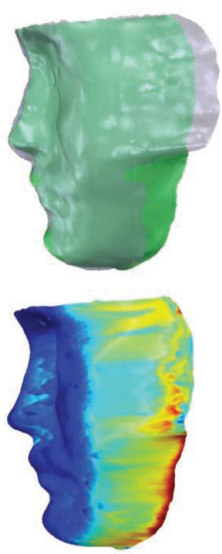
Counteracting Cannabis

What is the role of steroid hormones in vulnerability to addiction? Working with rodents, **Vallée *et al.*** (p. 94) found that all major drugs of abuse (morphine, cocaine, alcohol, nicotine) increase neurosteroid levels, with the active ingredient in cannabis (THC) inducing a particularly large increase. THC and other drugs increased levels of pregnenolone, long thought to be an inactive precursor of downstream active steroids. Pregnenolone antagonized most of the known behavioral and somatic effects of THC.

Improving Whole-Genome Screens

Improved methods are needed for the knockout of individual genes in genome-scale functional screens. **Wang *et al.*** (p. 80, published online 12 December) and **Shalem *et al.*** (p. 84, published online 12 December) used the bacterial CRISPR/Cas9 system to power-screen protocols that avoid several of the pitfalls associated with small interfering RNA (siRNA) screens. Genome editing by these methods completely disrupts target genes, thus avoiding weak signals that can occur when transcript abundance is partially decreased by siRNA. Furthermore, gene targeting by the CRISPR system is more precise and appears to produce substantially fewer off-target effects than existing methods.

Computing an Image



Firing off a burst of laser pulses and detecting the back-reflected photons is a widely used method for constructing three-dimensional (3D) images of a scene. **Kirmani *et al.*** (p. 58, published online 29 November) describe an active imaging method in which pulsed laser light raster scans a scene and a single-photon detector is used to detect the first photon of the back-reflected laser light. Exploiting spatial correlations of photons scattered from different parts of the scene allows computation of a 3D image. Importantly, for biological applications, the technique allows the laser power to be reduced without sacrificing image quality.

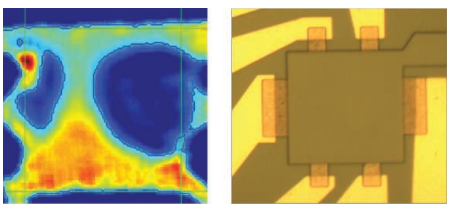
Familiarity Does Not Breed Contempt

Female mating preference is influenced by social familiarity in various species from fish to primates. **Okuyama *et al.*** (p. 91) showed in Japanese rice fish that females prefer to mate with visually familiarized males over unfamiliar males and that this preference is mediated by specific neuromodulatory neurons in the female brain.

Additional summaries

Exciton Liquid

Excitons, bound states of electrons and holes (states "vacated" by electrons), can be found in semiconductors and have long been predicted to form correlated phases at sufficiently large densities and low temperatures. **Stern *et al.*** (p. 55) studied the behavior of spatially indirect excitons, which consist of electrons and holes residing in



spatially separated, but coupled, quantum wells. The excitons were created through a combination of photoexcitation and electric gating. At high enough laser power and low enough temperatures, a new phase with a distinct photoluminescence signature appeared with behavior consistent with that of a classical liquid of excitons.

Guests for Conductors

Thin films of metal-organic framework (MOF) compounds are generally poor conductors because the linking organic groups are usually insulators with little π-orbital conjugation. **Talin *et al.*** (p. 66, published online 5 December) show that infiltrating films of the copper-based MOF HKUST-1 with the conjugated organic molecule 7,7,8,8-tetracyanoquinododimethane created an air-stable material with conductivities as high as 7 siemens per meter.

Why, Oh Y?

The mammalian Y chromosome is a symbol of maleness and encodes genes important for male reproduction. Various deletions of the Y chromosome result in sperm defects and infertility. When haploid male germ cells were injected directly into oocytes, **Yamauchi *et al.*** (p. 69, published online 21 November; see the Perspective by **Capel**) found that living offspring could be derived from male mice whose Y chromosome contribution was limited to only two genes. These two genes are the testis determinant factor *Sry* and the spermatogonial proliferation factor *Eif2s3y*.

Chromosome Condensation

The forces that shape the structure of the highly condensed metaphase chromosomes seen during cell division in eukaryotes are still largely unknown. In vitro evidence suggests that the amino-terminal tails of the histones—such as interaction of the histone H4 tail with H2A-H2B—play an important role in chromosome hypercondensation. **Wilkins *et al.*** (p. 77) used ultraviolet cross-linker amino acids in the histones of bakers' yeast to show that during early mitosis, phosphorylation of H3 threonine 3 by Haspin kinase recruits the chromosome passenger complex (CPC). The subsequent phosphorylation of H3 serine 10 by CPC allows the recruitment of the deacetylase Hst2p to nucleosomes. Hst2p drives the deacetylation of H4 lysine 16, facilitating the interaction between H4 and H2A-H2B in neighboring nucleosomes, promoting chromatin condensation.

DNA Damage Repair

In human cancers, oncogene activation interferes with DNA replication, leading to DNA replication stress and DNA double-strand breaks (DSBs). **Costantino *et al.*** (p. 88, published online 5 December) identified two subunits of DNA polymerase delta, POL3 and POL4, as critical for survival of DNA replication stress in human cells. Both subunits were required for break-induced replication (BIR), which is required to repair a specific type of DSB, with both subunits possibly required for processive DNA synthesis in BIR. Tandem head-to-tail duplications and fold-back inversions were seen in replication-stressed cells, similar to those seen in human breast and ovarian cancers, suggesting that BIR is important for repairing damaged forks in cancer cells.

CREDIT: STERN *ET AL.*