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Challenges facing broad-spectrum snakebite treatments

Every year, snakebites kill up to 90,000 people worldwide, mostly in impoverished, rural tropical areas. Because snake venoms vary widely, antivenoms effective against the bite of one snake species are often futile against bites of related species. The number of particular toxin genes in the genomes of venomous snakes influences venom composition, but Nicholas Casewell et al. (pp. 9205–9210) tested whether toxin gene expression in venom glands and venom protein production in six related viperid snakes—four species of saw-scaled vipers, the Saharan horned viper, and the puff adder—also influence the makeup of the snakes' venoms. The authors report that the transcribed fraction of genomic regions identified as toxin genes ranges from 44–70% in the six snake species, and the expressed fraction translated into venom proteins ranges from 35–52%, suggesting that gene and protein expression influences venom content across species. Further, venom-induced pathological changes, such as hemorrhage and coagulation, in mice varied as a function of venom content between snake species. More importantly, antivenom produced by immunizing sheep with the venom of one species of saw-scaled viper was ineffective at neutralizing in mice the venom of another species of saw-scaled viper, suggesting that even subtle differences in venom composition can render antivenoms powerless against the venoms of different species, according to the authors.— P.N.

Sochurek's saw-scaled viper (*Echis carinatus sochureki*), found near Sharjah, United Arab Emirates.

Titan's haze and exoplanet atmospheres

As extrasolar planets transit across their parent star, the wavelengths of light blocked out by the exoplanet and its atmosphere can yield information about the planet's atmospheric composition. Haze in a planet's atmosphere, however, may complicate such transit spectra analyses because hazes obscure deeper atmospheric layers. To examine the effect of haze on transit spectra, Tyler Robinson et al. (pp. 9042–9047) studied occultations of the sun by Saturn's moon Titan using observations from NASA's *Cassini* spacecraft. The authors found that high-altitude hazes can interfere with transit spectrum observations, limiting useful observations to the tenuous atmospheric layers above approximately 1 mbar. Additionally, the light-absorbing properties of hazes can create a strongly sloped transit spectrum. The results suggest that haze effects are much more complex than previously thought, which will influence current and future studies of exoplanet atmospheres, such as will be performed by NASA's *James Webb Space Telescope*. — P.G.

Split-gene system for hybrid wheat seeds

Plant hybridization via cross-pollination has helped increase yields of cereal crops such as rice and rye. Although hybrid wheat plants offer superior yields and growth characteristics, compared with their homozygous parents, researchers have been unable to devise an efficient biological sterility method that would block self-pollination and yet produce fully fertile hybrid seeds. Katja Kempe et al. (pp. 9097–9102) describe a hybrid wheat system that confers male sterility using a split-gene system to express the phytotoxic protein barnase. The technique divides and distributes the barnase coding information at two loci located on allelic positions of the host chromosome, thus emulating genes in a configuration known as "linked in repulsion." Complementation occurs by co-expressing the barnase fragments and splicing them together via ligation. In this manner, the authors report, the system can grow and maintain sterile male partners to cross with females, but the hybrids are fertile. Demonstrating a pollination control system based solely on genetic modifications to the female crossing partner, the study offers a means to produce hybrid wheat seeds amid concerns about population expansion and threats to global food security, according to the authors. — T.J.

Ears of the female plant display the typical "open floret" phenotype and contain no seeds. All hybrid progeny plants exhibit full fertility.

Identifying genomic targets of chemicals

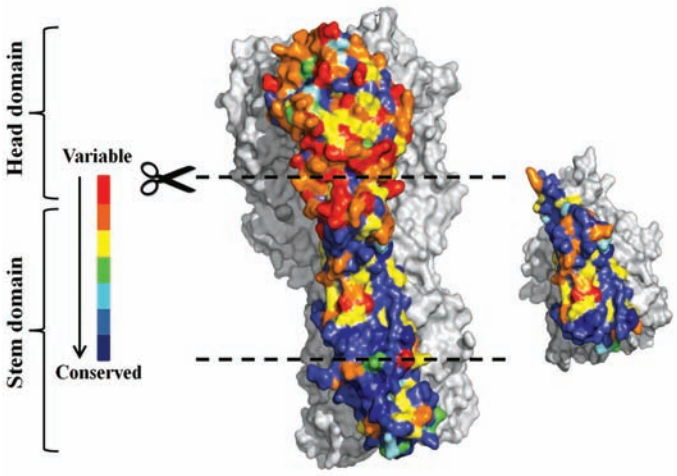
Over the last decade, researchers have devised a variety of strategies to uncover small molecules that function as drugs. However, the discovery of candidate drugs currently outpaces our ability to determine mechanisms of action. Chunyu Jin et al. (pp. 9235–9240) describe a novel approach that reveals the genomic targets and mechanism of action of a drug candidate initially identified by phenotypic screening. With a small molecule found by screening for inhibitors of ligand and genotoxic stress-induced translocations in prostate cancer cells, the authors mapped the candidate drug's genome-wide binding locations, which were revealed to be largely colocalized with enhancers of androgen receptors (AR), associated with cancer in prostate cells. Based on these findings the authors then conducted global analyses and ascertained that the candidate drug, dubbed SD70, inhibits AR signaling and prostate cancer cell growth. By providing a technique that maps small molecule activity across an entire genome, the approach might serve as an adjunct to contemporary drug development strategies, according to the authors. — T.J.

Early detection of lung cancer using MRI

Lung cancer leads to more than a million deaths per year, and less than 15% of lung cancer patients with non-small cell lung cancer (NSCLC) survive more than 5 years. To develop methods of early lung cancer detection, Andrea Bianchi et al. (pp. 9247–9252) administered nebulized ultrasmall gadolinium-based magnetic contrast agents to mice with nascent lung cancer, both intravenously and via the trachea. MRI revealed that the contrast agents congregated in tissues later shown to be lung tumors, identifying tumors less than 1 mm in diameter. The authors found that the method yielded improved results when the contrast agents were administered via the trachea, a delivery route that required lower doses of contrast agents than intravenous delivery. Previous studies of NSCLCs have used a systemic delivery route, and this study demonstrates the benefits of the orotracheal route, according to the authors. In contrast to other lung cancer diagnostic methods, MRI requires no ionizing radiation and is noninvasive. The results suggest that MRI, together with nebulized magnetic contrast agents, may provide a method for early detection and ongoing monitoring of lung tumors, according to the authors. — P.G.

Immunogen may help overcome hurdle to universal flu vaccine

In the quest to develop a universal flu vaccine, many researchers have homed in on the influenza hemagglutinin (HA) protein—the primary target of the humoral immune response to the virus. The protein's stem domain is an attractive target because it is conserved across influenza strains, but eliciting broadly neutralizing antibodies (bnAbs) against the stem is challenging in the presence of the protein's immunodominant and variable head domain. Vamsee Mallajosyula et al. (pp. E2514–E2523) designed a stem-derived immunogen that may circumvent this challenge by mimicking the native HA stem and enabling it to fold without the head domain. The authors report that the immunogen both binds to and elicits conformation-specific bnAbs that neutralize highly divergent Group 1 (H1, H5 subtypes) and Group 2 (H3 subtype) influenza virus strains in vitro. Further, the immunogen-elicited bnAbs competed with stem-directed human bNAbs for binding to HA, and possibly inhibit viral fusion with the host cell membrane during influenza virus entry. Stem immunogens designed from highly disparate strains of influenza protected mice against a lethal heterologous influenza virus challenge. According to the authors, the immunogens, which are thermotolerant and bacterially expressed in soluble form, may allow for rapid scale-up during a pandemic outbreak, even in resource-poor settings. — A.G.



Stemming flu by design.