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In This Issue

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Staph population genetics may reveal pathogenesis

Whole genome sequencing has helped researchers understand how viral pathogens evolve within their hosts. Compared with viruses, however, bacteria have larger genomes that replicate more faithfully and tend to conceal genetic variations that reflect population dynamics and functional adaptation within the host. Bernadette Young et al. (pp. 4550–4555) used whole genome sequencing to examine methicillin-resistant *Staphylococcus aureus* (MRSA), the bacteria responsible for a deadly, antibiotic-resistant hospital-acquired infection. The authors report that just eight mutations may underlie the transition from bacteria carried in an asymptomatic population to the bugs responsible for a fatal bloodstream illness. From a large cohort of subjects with nasally carried asymptomatic methicillin-sensitive *S. aureus* (MSSA), the authors charted the evolution of the bacterial population in an elderly patient who developed an *S. aureus* bloodstream infection 15 months after joining the study. When compared with two asymptomatic carriers, the authors found dynamic populations of staphylococci, harboring relatively few genetic variations that evolved measurably through time. Notably, the authors report, half of the mutations that distinguish the asymptomatic from bloodstream bacteria produce stop codons that truncate proteins prematurely and likely contribute to pathogenesis. The authors conclude that high-throughput sequencing may help researchers characterize bacterial genetic variation and evolution within the host. — T.J.

Image courtesy of Anna Dumitriu (Artist-in-Residence, Modernising Medical Microbiology Consortium).

The MRSA Quilt, a textile stained with bacteria grown on chromogenic agar, then autoclaved.

Hematopoietic stem cell precursors originate in yolk sac

Blood cells are so extensively mobile that researchers have been unable to pinpoint the developmental origin of the adult hematopoietic system. Yosuke Tanaka et al. (pp. 4515–4520) explored the longstanding question of whether nascent hematopoietic populations emerge from a single location during a discrete ontogenic event or from multiple ontogenic sources during an extended developmental period. The authors examined the nascent hematopoietic system in mice, focusing on the role of Runx1, a key transcription factor that regulates the development of adult hematopoietic system. The study revealed that blood progenitors and adult-type hematopoietic stem cells (HSCs) originate predominantly in the extraembryonic mesoderm of the yolk sac. The authors designed a mouse "embryo-rescue system" in which Runx1 was reactivated in Runx1-knockout conceptuses. Trials with the reactivation system, which the authors claim closely recapitulates the process of de novo hematopoiesis, revealed that Runx1 rescues the production of HSC precursors in the proximal region of the early yolk sac. These nascent cells, the authors report, then acquire the adult-type HSC phenotype later in gestation. The findings demonstrate that HSC production depends critically on Runx1 and pinpoints the cells' ontogenic source within the extraembryonic mesoderm, according to the authors. — T.J.

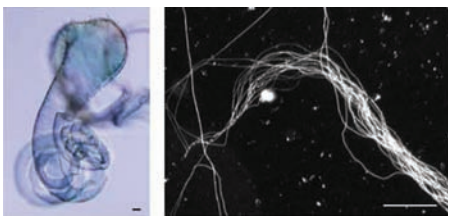
Tetrodotoxin-resistant garter snake (*Thamnophis sirtalis*).

Evolution of toxin resistance in distantly related snakes

Evolutionary adaptations to ecological challenges are assumed to be unpredictable because independent species have distinct histories and genetic material. But the functional constraints of biology might filter the spectrum of possible mutations to a limited set. Chris Feldman et al. (pp. 4556–4561) investigated the molecular mechanisms that allow six predatory snake species from around the globe to withstand a defensive toxin known as tetrodotoxin (TTX), secreted by a wide variety of amphibians. The findings reveal that only a small fraction of the possible mutations gave rise to the adaptation. Resistance to TTX, which selectively binds to the outer pore of the Nav1.4 ion-gated sodium channel, imposes a biophysical constraint that, according to the authors, might have helped molecular adaptations converge in disparate species. Further examination of sequence variation in the four domains that encode the Nav1.4 outer pore revealed that amino acid substitutions that reduced the affinity of TTX to the outer pore were less damaging to critical functions of the sodium channel than other mutations. The findings suggest that the functional consequences of amino acid replacements limit the spectrum of genetic variants that are available for adaptive evolution, according to the authors. — T.J.

How the female beetle's reproductive tract drives sperm evolution

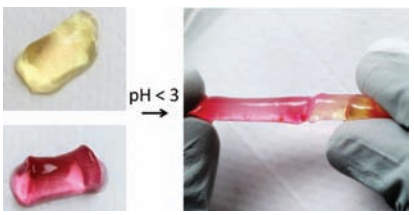
Darwin attributed the evolution of elaborate male traits to sexual selection exerted by females, but most studies have focused on outward, visible traits. Dawn Higginson et al. (pp. 4538–4543) investigated a less obvious characteristic: the morphological variation of sperm in the diving beetle, thought to have arisen due to postcopulatory selection by females. Comparative analysis of sperm from the aquatic beetles revealed diversity in physical characteristics such as length, head shape, and conjugation, or the union of two or more sperm for the purposes of motility or transport through the female reproductive tract. The authors also quantified female tract morphology for 42 species of diving beetles and found that variation in sperm morphology was significantly correlated with the size and shape of several female reproductive organs. Using statistical models to infer the probable sequences of evolution for sperm and the shape of the female tract, the authors found that the size and shape of several female reproductive organs and structures drive the evolution of different types of sperm. In particular, the authors showed that elongation of the female tract drives the loss of sperm conjugation. The present findings instead underscore the importance of postcopulatory sexual selection as an agent of diversification, according to the authors. — J.V.



Coevolution of female reproductive tracts (*Left*) and sperm morphology (*Right*) in the diving beetle.

Self-healing gels

Hydrogels are jelly-like materials that trap liquid in a tangled web of linked polymer molecules. Until recently, researchers have struggled to develop so-called self-healing hydrogels that can reknit broken molecular bonds after tear or damage. Ameya Phadke et al. (pp. 4383–4388) engineered a polymer's dangling side chain molecules to create a tough, self-healing hydrogel material. According to the authors, the flexible side chain molecules contain just the right size and number of water-soluble and water-repelling chemical groups to stretch across an interface and bond with the side chains of the nearby hydrogel. When the authors placed two cylindrical pieces of the hydrogel material in an acidic environment, the pieces welded to each other within seconds, and bonded strongly enough to withstand repeated stretching and exposure to boiling water. After many cycles of pH-mediated healing, separation, and rehealing, the material continued to repair itself on the same time scale and with comparable weld strength as the original undamaged material. In several proof-of-concept tests, the researchers showed that future uses for the material could include a sealant for vessels that contain corrosive acids, a tissue adhesive for stomach perforations, or a carrier for targeted drug delivery. — J.M.



Hydrogels capable of pH-mediated self-healing.