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In This Issue

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8841 Evolutionary selection of gene regulation
8877 Deceiving diones
8980 Color vision evolution in bats
9027 Malaria drugs exacerbate resistant infections
9039 Virotherapy for HER-2-positive cancers
9105 Turbulence and flight stability in orchid bees

PHYSICS, EVOLUTION

Evolutionary selection of gene regulation

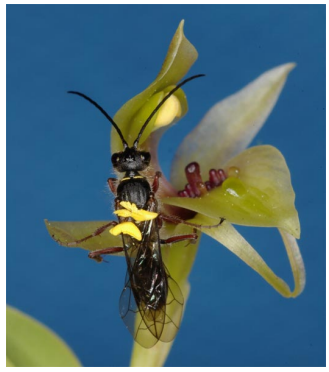
Switching on a gene typically involves either a transcription factor that binds to stimulate transcription, or a repressor that releases to allow transcription. In both cases, the regulatory protein responds to an external biochemical signal. Control theory assigns the label "double-positive" (++), to the regulation mode in which the signal activates a factor that activates the gene, and "double-negative" (−−), when the signal disables the repressor that deactivates the gene. One principle of bacterial evolution, called "use-it-or-lose-it," posits that (++) will evolve under high demand for a gene and (−−) under low demand, to avoid loss of function during periods when the circuit is not used. Another possibility, introduced by Ulrich Gerland and Terence Hwa, is a reverse situation called "wear-and-tear," in which high demand for a gene incurs a fitness reduction in the population if the regulation pathway is always on, because mutations are costly. The authors demonstrate that both use-it-or-lose-it and wear-and-tear are valid principles, but are separated by a transition that depends on population size and becomes sharper when the environment of a bacterial colony fluctuates on long timescales. — K.M.

"Evolutionary selection between alternative modes of gene regulation" by Ulrich Gerland and Terence Hwa (see pages 8841–8846)

BIOCHEMISTRY

Deceiving diones

Some orchid species mimic the female-produced sex pheromone of their pollinator species to attract males for pollination. Two species of Australian orchid, *Chiloglottis trapeziformis* and *C. valida*, use the pheromone 2-ethyl-5-propylcyclohexan-1,3-dione (chiloglottone1) to attract pollinator wasps *Neozeleboria cryptoides* and *N. monticola*, respectively. Previous research elucidated the structure of chiloglottone1 from gas chromatography/mass spectrometry data, which suggested a biosynthesis involving activated 3-oxohexanoic acid and 2-hexenoic acid. Stephan Franke et al. performed systematic investigations into the mass-spectrometric fragmentation of chiloglottone1 and similar reference compounds and identified 2 naturally occurring 2,5-dialkylcyclohexan-1,3-diones: 2-ethyl-5-pentylcyclohexan-1,3-dione (chiloglottone2) and 2-butyl-5-methylcyclohexan-1,3-dione (chiloglottone3) that the *Chiloglottis* orchids produce to attract pollinators. Field bioassays have demonstrated the bioactivity of the newfound diones to pollinators of the orchids. The authors suggest that 2-octenoate and 3-oxohexanoate form the likely building blocks of chiloglottone2, and chiloglottone3 is synthesized from crotonate and 3-oxooctanoate. Other *Chiloglottis* orchids appear to rely on specific blends of diones, the authors note, with the exact ratio of chiloglottones specific to a particular species of orchid. Because of their fatty acid biosynthesis, this recently identified class of natural compounds may be found in many different organisms, according to the authors. — C.A.



A *Neozeleboria* wasp pollinates a *Chiloglottis* orchid.

"The discovery of 2,5-dialkylcyclohexan-1,3-diones as a new class of natural products" by S. Franke, F. Ibarra, C. M. Schulz, R. Twele, J. Poldy, R. A. Barrow, R. Peakall, F. P. Schiestl, and W. Francke (see pages 8877–8882)

EVOLUTION

Color vision evolution in bats

The ability of bats to navigate in total darkness by echolocation is one of the hallmarks of the nocturnal winged mammal. Other nocturnal species have lost function of their visual genes because of relaxed selection pressures, but it remains unclear whether bats continue to rely on sight. Huabin Zhao et al. sequenced the visual cone opsin genes in 33 bat species and found that medium/long wavelength-sensitive (M/LWS) opsin genes were conserved in all bat species. The sequences also showed an intact open-reading frame and strictly conserved intronic splice sites, suggesting that M/LWS opsins remain functional in bats, perhaps because they aid in nonvisual functions, such as the regulation of circadian rhythms, according to the authors. The DNA sequences of the short wavelength-sensitive (SWS1) opsin gene, however, showed a divergent evolutionary pattern. Although echolocating bats with short emitted calls retained functional SWS1 opsins, those bats with long calls had a nonfunctional form of the gene. The

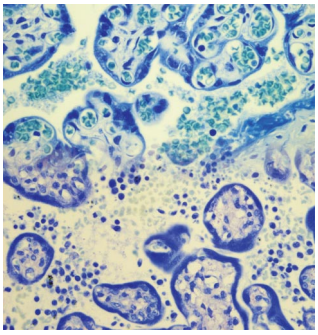
authors suggest that long-call bats may use echolocation to supplement vision in a dark environment, whereas the evolution of short-call echolocation may have rendered dichromatic color vision redundant. — C.A.

"The evolution of color vision in nocturnal mammals" by Huabin Zhao, Stephen J. Rossiter, Emma C. Teeling, Chanjuan Li, James A. Cotton, and Shuyi Zhang (see pages 8980–8985)

MICROBIOLOGY

Malaria drugs exacerbate resistant infections

To avert the deleterious effects of malaria infection during pregnancy, the World Health Organization recommends intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP). However, resistance to SP has emerged around the world, and previous research in mice has shown that treatment with pyrimethamine can increase the severity of malaria infections with mixed drug-resistance profiles. Whitney Harrington et al. found that Tanzanian women treated with SP IPTp carried more drug-resistant parasites and showed higher levels of parasitemia and inflammation in the placenta. Genetic analysis revealed that women with a history of SP IPTp had a higher percentage of parasites containing the DHPS 581 resistance allele compared to women with no history of IPTp. Higher incidence of parasitemia after IPTp suggests that elimination of susceptible parasites spurs the overgrowth of resistant parasites. Increased inflammation in the placentas of SP-treated women is associated with a greater likelihood of chronic malaria infections and increased risk for poor pregnancy outcomes. Preventive treatment with SP in regions with high malaria transmission and high drug resistance may increase the overgrowth of resistant parasites and worsen malaria infection, the authors say. — C.A.



Normal (*Upper*) and inflamed (*Lower*) placental tissue. Image courtesy of Atis Muehlenbachs.

"Competitive facilitation of drug-resistant Plasmodium falciparum *malaria parasites in pregnant women who receive preventive treatment" by W. E. Harrington, T. K. Mutabingwa, A. Muehlenbachs, B. Sorensen, M. C. Bolla, M. Fried, and P. E. Duffy* (see pages 9027–9032)

MICROBIOLOGY

Virotherapy for HER-2-positive cancers

Oncolytic virotherapy uses engineered viruses, such as herpes simplex viruses (HSVs), to infect and kill tumor cells while leaving healthy cells intact. The HER-2 surface protein, overexpressed in ≈25% of breast and ovarian carcinomas, is a clinically meaningful target for engineered HSVs, as elevated levels of the protein are correlated with high levels of malignancy and metastasis. Laura Menotti et al. engineered an HSV to target and lyse only HER-2–positive cancer cells. The authors targeted the HSV receptor-binding virion glycoprotein gD to HER-2–positive cells by deleting the core of gD and inserting an anti-HER-2 antibody. The engineered HSV (R-LM249) infected HER-2–positive ovarian cancer cells at a high rate. R-LM249 was cytotoxic for HER-2–positive cells, but not HER-2–negative cells. Intratumoral administration of R-LM249 in mice with HER-2–positive malignancies resulted in a significant proportion of tumor-free mice that remained stable 5 months after the last treatment. Targeted HSVs may one day be a treatment option for malignancies resistant to surgery and radio/chemotherapies, for brain metastases unreachable by monoclonal antibody treatments, and for otherwise untreatable tumors (e.g., glioblastomas) suitable for intratumoral administration of the engineered virus, according to the authors. — C.A.

A chimeric HSV glycoprotein gD targets HER-2–positive cancers.

"Inhibition of human tumor growth in mice by an oncolytic herpes simplex virus designed to target solely HER-2-positive cells" by Laura Menotti, Giordano Nicoletti, Valentina Gatta, Stefania Croci, Lorena Landuzzi, Carla De Giovanni, Patrizia Nanni, Pier-Luigi Lollini, and Gabriella Campadelli-Fiume (see pages 9039–9044)

PHYSIOLOGY

Turbulence and flight stability in orchid bees

Orchid-pollinating, neotropical euglossine bees traverse long distances and a variety of habitats as they forage for food. These bees must contend with aerial wind turbulence during flight, which can vary temporally and spatially, as well as between habitats. Stacey Combes and Robert Dudley measured the effects of aerial turbulence on forward flight and maximum flight speed in *Euglossa imperialis* males by using high speed video. At intermediate flight speeds, the bees demonstrated a significant side-to-side rolling motion that increased with forward speed until bees could no longer maintain flight stability. Bees extended their hindlegs ventrally at high flight speeds, increasing their moment of inertia and enhancing stability, at the cost of increased body drag and energy expenditure. Stability and maximum flight speeds varied widely between individuals, and only 20% of this variance was explained by body mass. Bees were able to maintain greater stability and reach higher flight speeds when the level of turbulence was experimentally reduced. Aerial turbulence can influence a bee's stability during flight and may affect its ability to forage in different habitats, according to the authors. — C.A.

Euglossine bees forage for nectar.

"Turbulence-driven instabilities limit insect flight performance" by Stacey A. Combes and Robert Dudley (see pages 9105–9108)