

DEVELOPMENT

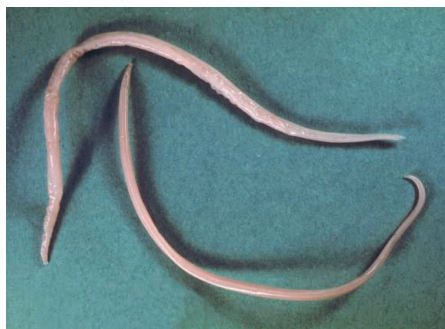
A Dish of Pancreas

Many cell lines of induced pluripotent stem cells (iPSCs) have been generated from tissue taken from patients with various medical conditions. The aim has been to use these as model systems ("disease in a dish") to study the biology of pathogenesis; as the iPSCs differentiate, cellular phenotypes characteristic of the early stages of the disease can reappear. At present, the prognosis of individuals with pancreatic ductal adenocarcinoma (PDAC) is poor, with a survival rate of less than 5%, and early diagnosis is rarely achievable. Furthermore, the available mouse and human cell models do not recapitulate the early stages of progression of this cancer. Kim *et al.* have now generated an iPSC line from a late-stage human pancreatic cancer. The cells resemble the human cancer cells in morphology and histology, and when these cells were injected into immunodeficient mice, pancreatic intraepithelial neoplasia lesions progressed to invasive PDAC. An analysis of these cells identified proteins that are secreted or released, as well as networks, such as TGF β 1 and integrin signaling. In particular, the HNF4A pathway is specific for early to intermediate stages of progression. — BAP
Cell Reports **3**, 10.1016/j.celrep.2013.05.036 (2013).

BIOMEDICINE

Without Worms Within

Some humans share several characteristics with pigs, including very similar parasitic worms. *Ascaris* spp. roundworms are large, pungent, and can occur in sufficient numbers to block the gut, pierce the peritoneum, and invade the bile duct. In children, the morbidity caused by a heavy worm infection can have lifelong consequences. Surprisingly perhaps, roundworms can be killed by a *Bacillus thuringiensis* (Bt) toxin a bacterium more usually encountered in crop pest control. Urban *et al.* have been exploring the potential of one Bt toxin, Cry5B, as an anthelmintic (a deworming drug), using young pigs as a human substi-



ENVIRONMENT

Unintended Consequences

Half a century ago, in what probably seemed like an entirely beneficent central planning program, coal for winter heating was provided free of charge to homes north of the River Huai in China for several decades. Burning this coal released particulate matter that contributed to a decline in air quality. Through a painstaking accumulation of data on suspended particulates in the 1980s and 1990s, coupled to a regression discontinuity design—in essence, assuming that unobservable parameters change smoothly from one side of the river to the other and checking to ascertain whether observable parameters obey this assumption—Chen *et al.* are able to demonstrate that the concentration of particulates shifts abruptly from about 400 mg/m³ on the south side to 600 mg/m³ on the north bank. What is rather worrisome is that they also find that life expectancy drops by about 5 years when crossing the river from south to north. The higher mortality rate is due to an increase in cardiorespiratory disease, such as stroke and lung cancer, and not to other cancers. — GJC
Proc. Natl. Acad. Sci. U.S.A. **110**, 10.1073/pnas.1300018110 (2013).

tute. Experiments on the mode of action in the classic worm model *Caenorhabditis elegans* showed that Cry5B binds to galactose-containing glycolipid receptors found only in invertebrates, and this was confirmed to be the case in *Ascaris*, too. Cry5B was given by gavage to groups of five piglets as spore crystal lysate in two doses (20 mg/kg) at 10 and 12 days after infection, when the penultimate larval worm stage emerges into the gut (unfortunately, there are severe practical constraints on testing the limited-availability Bt toxin on the slow-growing adult worms), and 6 days later, 97% of these larvae were dead and the remainder disabled. The natural product Cry5B could thus be a valuable addition to the anthelmintic roster, especially as resistance is emerging to the standard drugs. — CA
PLoS Negl. Trop. Dis. **7**, e2263 (2013).

ASTRONOMY

A Captured Black Hole?

NGC 1277, a compact lenticular galaxy located in the Perseus Cluster, hosts a black hole 17 billion times as massive as the Sun. Most galaxies are thought to have a massive black hole at their centers, but it usually represents only 0.1% of the mass of the stellar bulge of the galaxy. The black hole in NGC 1277 accounts for 59% of the stellar bulge mass. Shields and Bonning propose that such an overweight black hole did not form in NGC 1277 but was instead captured from another, much larger galaxy, where ultra-massive black holes are more likely to form. They suggest that the black hole formed through the merger of two giant elliptical galax-

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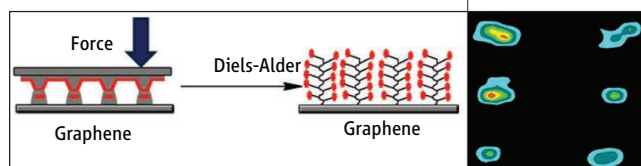
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ies, each containing a massive black hole. The inspiral of the two black holes resulted in the ejection of the larger black hole produced by merger. The ejected black hole then wandered in the core of the cluster until it got captured by NGC 1277 during a chance encounter. — MJC
Astrophys. J. **772**, L5 (2013).

CHEMISTRY

Forcing Patterns onto Graphene

The Diels-Alder reaction is used to create ring compounds between dienes and dienophile, which include a variety of substituted alkenes. A recent study showed that double bonds in the graphene surface can also act as dienophiles at elevated temperatures (50°C). Bian *et al.* harnessed this reactivity for patterning single-layer graphene supported on silica surfaces. They synthesized diene-bearing molecules—cyclopentadiene molecules functionalized either with a Raman-active dye or with electrochemically active ferrocene—and created an ink of these molecules with polyethylene glycol (PEG). They then loaded this ink onto an elastomeric tip array that was mounted on an atomic-force microscope tip and used it to write patterns. The Diels-Alder reaction has a negative activation volume and speeds up at elevated pressure. When sufficient force was applied with the elastomeric tips, the graphene reaction proceeded at room temperature. After washing off the PEG and unreacted molecules,



they imaged the patterns with Raman microscopy and observed changes in characteristic graphene bands indicative of covalent bonding at the surface. Cyclic voltammetry studies revealed a much higher coverage than would be expected from the density of reactive double bonds on graphene. The authors suggest that cyclopentadiene is undergoing further oligomerization reactions under these conditions. — PDS

J. Am. Chem. Soc. **135**, 9240 (2013).

SIGNAL TRANSDUCTION

Piping Calcium Around

Understanding the dynamic interactions of the components of signaling networks that control cell function is a central challenge for systems biology. Bandara *et al.* have adapted a strategy from engineers to get a better understanding of the controllers of free calcium concentrations in

the cytoplasm and the endoplasmic reticulum; active and passive ion channels, pumps, and other regulatory proteins adjust the calcium levels in these intracellular compartments. Modeling such a system is confounded by incomplete characterization of the various components and variations in the responses of single cells in a population. The authors thus characterized the system with ordinary differential equation models built from detailed time-course measurements from large numbers of individual cells. This allowed them to extract estimates of key parameters and identify those most important to the cellular response. The results revealed the role of presenilin—a protein linked to Alzheimer's disease—in calcium handling and defined a feedback loop that controls the extrusion of calcium. — LBR

Sci. Signal. **6**, ra56 (2013).

EDUCATION

Modeling Conceptual Understanding

Reforms in biology education aim to develop students' understanding of biological processes in the context of systems, both within and across spatial and temporal scales. Concept maps are useful in this regard because they allow students to model their conceptual understanding in a hierarchical manner. Dauer *et al.* describe changes

in student-constructed "Gene-to-Evolution" models over a semester of an introductory biology course in order to characterize changes in students' thinking about the genetic

basis of evolution. Models were evaluated on the number of structures and relationship branches presented, as well as the quality of language used to describe them. In the first half of the course, models progressed from simple linear structures to complex ones with branches and connections. Over the second half of the course, the architecture of the models declined while the amount of correct information presented in the models continued to increase, suggesting that over time students were able to replace irrelevant information with appropriate language and relationship connections. These results suggest that learning a skill such as concept mapping should not be considered as a remedial activity, but rather as a skill that helps students improve systems thinking through a focus on conceptual relationships and the use of biological language. — MM

J. Res. Sci. Teach. **10.1002/tea.21094** (2013).