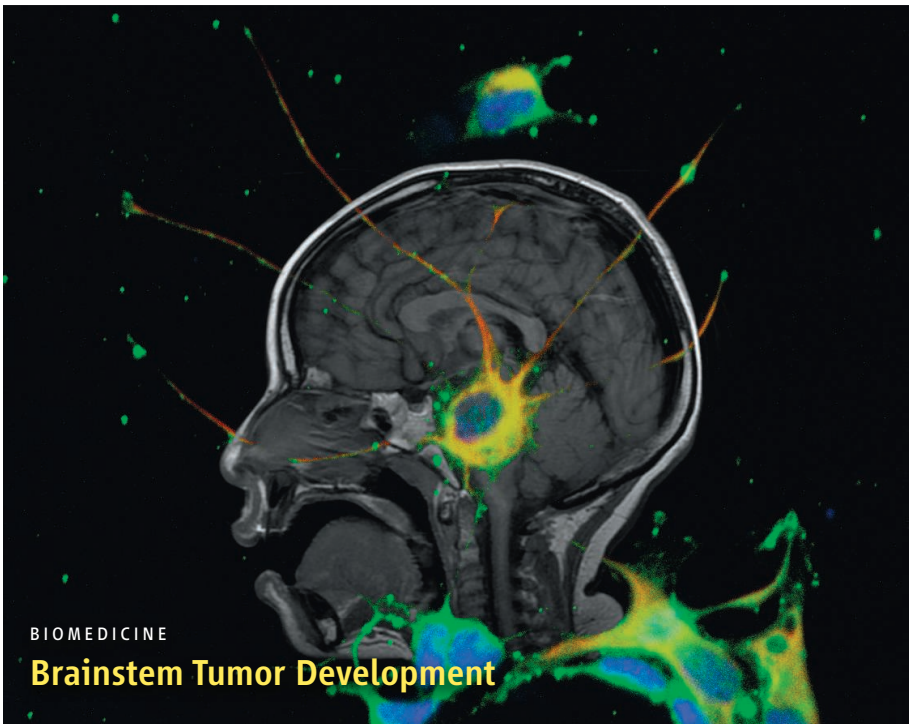


CREDIT (LEFT): MONJE ET AL., PROC. NATL. ACAD. SCI. U.S.A. 108, 10.1073/PNAS.1101657108 (2011). (DIPG IMAGE) MORGAN FRETET AND PHIL BEACHY; (RIGHT) NASA (FULL CREDIT INFORMATION AVAILABLE AT HTTP://APOD.NASA.GOV/APOD/AP060824.HTML)



BIOMEDICINE

## Brainstem Tumor Development

Brain cancer is the most common solid tumor in children. For children with medulloblastoma, survival rates have steadily improved as a result of optimized therapies. In contrast, children with an aggressive brainstem tumor called DIPG (for diffuse intrinsic pontine glioma) are far less fortunate, with death occurring usually within a year. Because biopsy specimens of human DIPG are rare and because there are no relevant animal models, little is known about the cellular and molecular origins of these tumors.

A study by Monje *et al.* provides insight both into the likely cell of origin of DIPG and into a signaling pathway that may help promote tumor growth. The culprit cell appears to be a previously uncharacterized neural precursor cell in the normal human brainstem. The density of these cells peaks during the time of childhood, when DIPGs most commonly arise. In a cell culture model, human DIPG cells (above, overlaid on an MRI scan from a DIPG patient) showed activation of the Hedgehog (Hh) signaling pathway, which is critical to normal brain development and which is aberrantly activated in other human cancers, including medulloblastoma. Thus, DIPG probably arises through dysregulation of postnatal neurodevelopment, and the Hh signaling pathway may be a possible therapeutic target for this tumor. — PAK

*Proc. Natl. Acad. Sci. U.S.A.* **108**, 10.1073/pnas.1101657108 (2011).

EPIDEMIOLOGY

## Tracking a TB Network

Improvements in two very different methods of investigation led to better understanding of the dynamics of a tuberculosis (TB) outbreak in British Columbia, Canada. A 10-fold increase in TB cases was reported in a Canadian community between 2006 and 2008. Initial genotyping analysis by Gardy *et al.* suggested that the outbreak was clonal; however, whole-genome sequencing of *M. tuberculosis* isolates produced a different picture: The cases were the result of two outbreaks. Examination of historical isolates

indicated that the two lineages were present before the recent outbreak, which suggested that it was a social or environmental effect, not a genetic mutation, which triggered the increase in cases. Social network analysis was then used to build a picture of risk behavior, interactions, and social meeting places. When this was combined with the whole-genome data, the investigators were able to identify sources of the outbreak and a likely contribution of increased crack cocaine use. As



sequencing costs go down and network analyses become more sophisticated, it is likely that these strategies will be increasingly used in public health efforts. — BJ

*N. Engl. J. Med.* **364**, 730 (2011).

BIOMEDICINE

## Lupus Casts a Complicated NET

Systemic lupus erythematosus is a debilitating autoimmune disease that is characterized by the accumulation of inflammatory immune complexes (antibodies bound to a person's own nuclear structures) in tissues. Lupus patients exhibit alterations in cytokine production and in various immune cell numbers and functions, but how these changes contribute to disease pathogenesis is not well understood. Lande *et al.* and Garcia-Romo *et al.* analyze serum samples and cells isolated from lupus patients and report that immune complexes, type I interferons, and neutrophils are entwined in a vicious cycle that drives disease pathogenesis. This trio of immune mediators is elevated in lupus serum, and together they induce a type of cell death in neutrophils called NETosis, where neutrophils spew out their nuclear contents (NETs). NETs drive further production of interferons, which in turn induces more NETosis. NETs are also an antigenic source for the generation of more immune complexes. With only one targeted therapy available for lupus, new therapeutic targets such as these are badly needed. — KLM

*Sci. Transl. Med.* **3**, 73ra19; 73ra20 (2011).

ASTRONOMY

## Bullets in the Dark

Dark matter, amounting to 85% of the matter of the universe, interacts with ordinary matter through gravity and possibly through the weak nuclear force. Massey *et al.* propose a statistical method that could help constrain the extent to which dark matter and ordinary matter interact via the weak force. When two clusters of galaxies collide, as happened in the Bullet cluster, the gas composing most of the ordinary matter in

the clusters is slowed down by drag forces, temporarily separating from the dark matter, which passes unimpeded through the collision. The degree of separation reflects the degree

*Continued on page 1495*

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of interaction of dark matter, but constraints are limited by the rarity of cluster collisions. Numerical simulations of cosmic structure formation tell us that clusters are built gradually from smaller pieces of infalling matter. The new method treats these pieces as bullets, whose ordinary matter is expected to drag behind the dark matter. Although individual separations between ordinary and dark matter may not be significant, averaging through a large number of clusters could provide constraints that are tighter than those provided by the collision in the Bullet cluster. — MJC

*Mon. Not. R. Astron. Soc.* 10.1111/j.1365-2966.2011.18246.x (2011).

## CHEMISTRY

### Negative Get-Togethers

When transition-metal salts dissolve in water, it's not unusual for a number of the counterions to remain coordinated. In contrast, alkali metal ions such as sodium or potassium weren't traditionally thought to behave this way; dissolution of their salts conjures images of a sea of water molecules keeping anions and cations thoroughly apart. Recently, however, precise spectroscopic studies have been uncovering a more complicated scenario for these simple salts, in which cation and anion continue to influence one another in solution. In one such study, Bian *et al.* now present evidence that concentrated solutions of alkali thiocyanates (SCN<sup>-</sup>) exhibit anion clustering. The authors used two-dimensional infrared spectroscopy to measure vibrational energy transfer between isotopically light and heavy SCN<sup>-</sup> solutes as a probe of their proximity, and they found that in 10 M KSCN, over 90% of the anions gathered in clusters. Rotational anisotropy measurements implicated cluster sizes of approximately 18 anions. Diluting the solution reduced the apparent proportion of anions that gathered in clusters, as did shifting to smaller cations (lithium or sodium); cesium—the largest stable alkali—correspondingly induced the highest clustering proportion. — JSY

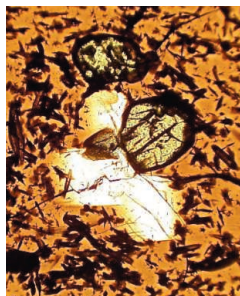
*Proc. Natl. Acad. Sci. U.S.A.* 108, 10.1073/pnas.1019565108 (2011).

## GEOCHEMISTRY

### Under the Ridge

Oceanic crust forms along the spine of mid-ocean ridges—massive mountain chains along the seafloor—which churn out lava and push fresh crustal material outward in both directions. Discerning how the hot material delivered from the subsurface to the ridge eventually turns into

crust depends on quantifying the cooling rate of fresh lavas. In search of new geochemical clues to constrain heat transfer processes, Schmitt *et al.* sampled lavas from a segment of the Juan de Fuca ridge off the coast of western North America. From the rock samples collected (such as the dacite shown below), they separated tiny



crystallized zircon grains, which serve as an excellent thermometer for tracking the thermal history of the melts. Dates obtained using a variety of radiometric dating techniques translate to rapid cooling rates: over

an order of magnitude faster than crust formed along other segments of the same ridge. These rates are too fast to support models by which the crust cools via conduction, instead implicating cooling by permeation of convective hydrothermal fluids through the new crust. — NW

*Earth Planet. Sci. Lett.* 302, 349 (2011).

## CELL SIGNALING

### Cell Signaling Goes Live

Elucidation of cellular signaling pathways holds the promise of revealing new therapeutic targets. Such an approach, however, requires a deeper understanding of how signaling pathways interact in regulatory networks and within their physiological niche *in vivo*. Lau *et al.* studied effects of the cytokine TNF- $\alpha$ , which contributes to chronic inflammation in diseases such as inflammatory bowel disease. TNF- $\alpha$  administration to mice caused apoptosis of epithelial cells in the duodenum, whereas further along the small intestine in the ileum, TNF- $\alpha$  induced proliferation. By characterizing the phosphorylation signals from proteins known to act as critical nodes in cell signaling pathways, the authors constructed mathematical models of the variation in responses to TNF- $\alpha$ . These models predicted that the protein kinase ERK may regulate the distinct regional responses. Pharmacological inhibition of ERK signaling confirmed the predictions and showed that modulation of ERK signaling affected the signaling network beyond the ERK pathway itself. The results show an effective strategy to characterize complex *in vivo* responses through modeling and then test predictions experimentally, a method that may enhance the development of new therapeutic strategies. — LBR

*Sci. Signal.* 4, ra16 (2011).