Malaria parasites invade and feed within human red blood cells and can cause high rates of mortality if untreated. Consequently, and as hypothesized by Haldane, in recent human history malaria has selected for several hemoglobin mutations with distinctive patterns of global distribution, which hinder the parasite to different degrees. Penman et al. have investigated the population genetics of the contrasting distributions of hemoglobin mutations associated with thalassemias (which exhibit quantitative deficiencies in $\alpha$- and $\beta$-globin synthesis that can provide up to 60% protection against malaria) in the Mediterranean, and those of sickle cell anemia (a structural defect in $\beta$-globin that confers in excess of 90% malaria protection) in sub-Saharan Africa. The authors suggest that the distinct geographies reflect an active exclusion of the sickle-cell mutation from Mediterranean populations as a result of intracellular interactions between the $\alpha$- and $\beta$-globin variants. The pathophysiology of the thalassemias is caused by an imbalance in the globin subunits; several mutations coexist, and if an individual inherits two different thalassemia mutations, the imbalance may be ameliorated without any loss of the malaria-protective effect. In contrast, co-inheritance of an $\alpha$ thalassemia with sickle cell anemia ablates any malaria-protective effect and transmits a double whammy of hemoglobinopathy and malaria risk to the afflicted individual. — CA

_Haldane’s Hemoglobin Hypothesis_

**CELL BIOLOGY**

**A Message in a Vesicle**

When cells undergo programmed cell death, small portions of the plasma membrane pinch off and form microvesicles known as apoptotic bodies. Zerneck et al. show that apoptotic bodies carry a message from the dying cells to healthy ones that promotes the repair of atherosclerotic lesions. Apoptotic bodies from dying human umbilical vein endothelial cells were taken up by healthy endothelial cells and increased expression of the gene encoding CXCL12, a chemokine that recruits progenitor cells to sites of repair. The active component of the apoptotic bodies was not a protein but the microRNA miR-126, which inhibited the translation of the mRNA encoding an inhibitor of signaling via CXCR4, which is the receptor for CXCL12 and also enhances its expression. In a mouse model of atherosclerosis, administration of apoptotic bodies or miR-126 promoted the production of CXCL12 and reduced the size of lesions in the blood vessels. — LBR

Sci. Sig. 2, ra81 (2009).

**DEVELOPMENT**

**Bounded Excitement**

Brain development is characterized by shifting patterns of gene expression and by gradients of cell differentiation. Scholpp et al. have analyzed the zebrafish thalamus to understand how one such gradient defines neuronal phenotype. Proteins of the Hes/Her family repress transcription of their target genes, which in some cases keeps a neural progenitor cell in its precursor state. Initially, her6 is expressed throughout the developing thalamic region. Cells in the rostral thalamus, which maintain her6 expression longer, normally develop into inhibitory GABAergic neurons, whereas cells in the caudal thalamus, from which her6 expression recedes earlier, begin to express neurog1 and develop into excitatory glutamatergic neurons. Overly persistent expression of her6 in the caudal thalamus suppresses neurog1 and induces those cells to develop into GABAergic neurons. Thus, the shifting pattern of her6 expression defines separate identities for these two thalamic regions. — PJH


**EDUCATION**

**Elementary Partnership**

The Elementary Science Education Partnership (ESEP) was created to bring elementary school teachers into working partnerships with science-literate college students, who would carry their knowledge, confidence, and enthusiasm for science into the teachers’ classrooms. Goebel et al. report the implementation and preliminary impact of the program. ESEP hired experienced educators and administrators to guide the professional development of the classroom teacher mentors, including instruction at summer institutes in both the science content and pedagogical strategies required to teach a science kit. These teacher mentors, called SKIL teachers, went on to train their colleagues at their home schools. Undergraduates completed a one-semester course where they learned inquiry-based approaches to science learning and
science pedagogy. For one semester, undergraduate and teacher pairs committed 3 to 4 hours per week to hands-on activity in the classroom. It became an honor among teachers and administrators to be chosen to participate in the program. Evaluation showed that teachers mentored by SKIL teachers were better able to design and implement lessons and were more capable of conveying scientific subject matter than those who were not mentored. Undergraduates also reported gains in their own understanding of science as a result of having taught basic elements. — MM


PHYSICS

Racing Down the Table

Accelerating particles to very high energy is usually done at large national facilities with the aim of smashing atoms to probe their constituent parts. Accelerators on a smaller, but still rather grand, scale find use in biomedical applications such as cancer treatment. The availability of high-intensity laser pulses to manipulate electrons offers the possibility of shrinking the size of particle accelerators even further. However, the demonstrations of laser-based acceleration so far have been at large laser facilities and have involved pulses produced at a low repetition rate. Mordovanakis et al. report a technique to produce electrons at faster repetition rates, using a double pulse setup whereby a moderate prepulse (~10¹⁴ W cm⁻²) is focused onto a target before the arrival of the main pulse (10¹⁸ W cm⁻²). By varying the delay time between the prepulse and the main pulse, the authors can control the 500-Hz production of quasi-monoenergetic electron pulses at relativistic energies (0.8 MeV), thereby offering the prospect of tabletop accelerators. — ISO


BIOCHEMISTRY

Cobalt Ins and Outs

Vitamin B₁₂ (cobalamin) has been cited prominently in the history of the Nobel Prizes, for its contributions to pernicious anemia, organic synthesis, and crystallography. Methylmalonyl-CoA mutase (MCM) is one of only two mammalian enzymes that rely on cobalamin, and Padovani and Banerjee describe the intricate mechanisms for ensuring that active cofactor is loaded onto MCM and inactive cofactor is removed. A trimeric adenosyltransferase (ATR) turns inactive cobalamin into the active AdoCbl form by adding the deoxyadenosine moiety derived from ATP. Only two of the three sites are occupied by AdoCbl molecules, and binding of the substrate ATP to the empty site is used to eject one AdoCbl in the fashion of a rotary motor. A second nucleotide-driven step is regulated by the G protein chaperone MeaB, which mediates a tripartite exchange between ATR and MCM; the binding energy of GTP is used to select in favor of the active AdoCbl versus cobalamin itself, and the hydrolysis energy of GTP is used to promote the release of inactive cofactor from MCM, which can occur during MCM turnover. Finally, a human mutation in MCM that has no effect on enzyme activity per se was shown to block the editing capacity of MeaB, providing a mechanistic explanation for methylmalonic aciduria in this patient. — GJC


MATERIALS SCIENCE

Plated Pillars

Mechanical testing of submicrometer-sized metal pillars has shown significant strengthening on decreasing the pillar dimensions. Analysis of such experiments is complicated, however, because the traditional focused ion beam method for making the pillars causes damage through the implantation of Ga⁺ ions and leads to vertical tapering. Burek and Greer turned to lithographic techniques, using an electron beam to pattern a poly(methylmethacrylate) (PMMA) film. The patterned film was in turn used to template pillar growth by deposition of gold or copper through electroplating. The plating conditions could be tuned to vary the microstructure of the pillars, which ranged from single crystals to twin domain and highly nanocrystalline structures. Pillars for compressive testing were fabricated by halting plating before reaching the top of the PMMA layer; for tensile testing, the pillars were overplated with a cap to facilitate gripping of the sample. The pillars showed little tapering and exhibited diameters as small as 25 nm, much smaller than the lower limit attainable by a focused ion beam. — MSL

Nano Lett. 10.1021/nl902872w (2009).