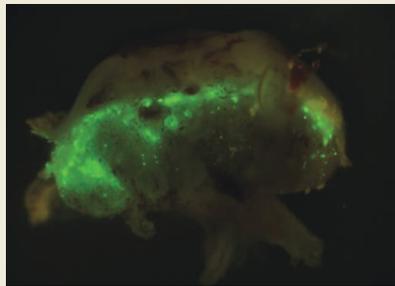


DEVELOPMENT

Surviving Methyl Deficiency

The blastocyst of mammalian embryos includes an inner cell mass, which goes on to form the embryo proper, and the trophoblast layer, which forms extraembryonic tissues, such as the placenta. In normal development, DNA methylation is crucial, but these modifications are erased in the zygote and reestablished during subsequent rounds of cell division. Recent work in mice showed that embryonic stem cells (derived from the inner cell mass) do not need the three DNA methyltransferases (Dnmt1, Dnmt3a, and

Dnmt3b). Sakaue *et al.* now demonstrate that a differentiated cell type of the extraembryonic lineage can also dispense with them. When methyltransferase-deficient mouse embryos were generated via nuclear transfer technology, cells ap-



appeared normal up to the blastocyst stage (top). Later, cell death was seen in embryonic cell lineages, whereas typical extraembryonic lineages (green just above) were observed. This finding indicates that the mouse epiblast lineage can be specified without DNA methylation but that these cells do not persist; in contrast, extraembryonic cells do differentiate, and trophoblastic stem cells can be established in the absence of zygotic DNA methylation. At this point, the reason for this divergent requirement in these lineages for epigenetic modification is unknown. — BAP

Curr. Biol. **20**, 1452 (2010).

EDUCATION

They Aren't Just for E-mail?

Proficiency in navigating operating systems, data files, and analysis software is essential to being a successful scientist. To this end, 12 students majoring in biology at Emory University recently enrolled in the inaugural "Computer Literacy for Life Sciences" course. As Smolinski reports, the course was divided into four separate modules that took students through a virtual research project. "Operating Systems and Web-based Project Repositories" familiarized students with two operating systems, Windows and Unix/Linux. "Databases and Data Querying" covered the basics of relational database management systems and protocols for obtaining desired portions of data. "Data Analysis" dealt with various statistical programs and spreadsheets, mainly Excel and the more sophisticated statistical analysis package known as SPSS. Finally, "Presentation of Scientific Discoveries" offered students the chance to summarize their virtual research project in the form of a short journal article and presentation. Course surveys and evaluations showed positive feedback from the students. — MM

CBE Life Sci. Educ. **9**, 357 (2010).

ANTHROPOLOGY

Eastward Ho!

Researchers have debated the timing and pace of the human colonization of the Americas, though it seems clear that a migration of Paleoindians into northeast Asia came first. The record of sites in this region should thus form a basis for

evaluating the subsequent crossing into Alaska. Hamilton and Buchanan synthesize radiocarbon dates from nearly 150 sites across northern Eurasia and Alaska, ranging in age from about 45,000 to 11,000 years, and infer the expansion dynamics of modern humans into Alaska as well as Japan and Korea. Sites older than about 40,000 years appear only in southern Siberia; Japan, Korea, and much of the rest of Eurasia up to the western edge of Beringia (dashed line in the graphic) contain sites at least as old as 30,000 years. Afterward, there seems to have been a lull in expansion northward, coincident with the coldest temperatures and peak glacial expansion of the last Ice Age. Sites only appear within Beringia after about 16,000 years ago. The data support an overall slow rate of expansion of about 0.16 km/year and imply that North America was colonized only after the last glaciation. — BH

PLoS ONE **5**, e12472 (2010).



BIOMEDICINE

Chippin' Away at Vitamin D

Every week seems to bring another epidemiological study linking vitamin D deficiency to an elevated risk of disease. The expanding list of diseases extends well beyond the bone disorders that made vitamin D famous, and includes autoimmune disorders, cancer, and cardiovascular disease. Given that 1 billion people worldwide are estimated to suffer from vitamin D deficiency or insufficiency, the biological pathways by which vitamin D acts are of great interest. Ramagopalan *et al.* have catalogued the number and

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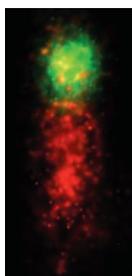
types of human genes that are likely to be regulated by vitamin D via its receptor VDR, which is a transcription factor. Applying a technique called ChIP-seq (chromatin immunoprecipitation followed by massively parallel DNA sequencing) to human lymphoblastoid cells, they found that VDR bound to 2776 genomic sites in response to vitamin D signaling and that 229 genes showed significant changes in expression as a result. Interestingly, VDR binding sites were enriched near several candidate genes that have been previously implicated in autoimmune disorders and certain cancers, suggesting that further investigation of this subset of genes may be revealing about the role played by vitamin D in disease pathogenesis. — PAK

Genome Res. **20**, 10.1101/gr.107920.110 (2010).

CELL BIOLOGY

This Bud's 4U

The reconstitution of membrane trafficking events in cell-free systems has contributed to understanding the mechanisms of vesicle targeting to and fusion with membranes.



Wu *et al.* have now reconstituted endocytic budding from plasma membrane sheets. Fluorescently labeled mammalian cell plasma membranes were incubated at 37°C in the presence of cytosol, ATP, and either GTP or its nonhydrolyzable analog GTP- γ -S. In the presence of GTP- γ -S, the plasma membrane invaginated into numerous clathrin-associated tubules as large as 2 μ m in length, and the subsequent addition of GTP led to the release of numerous vesicles. A protein known to promote membrane tubulation, FBP17 (red), associated with the GTP- γ -S-generated invaginations, as did clathrin (green) and dynamin. Blocking clathrin assembly blocked the production of membrane invaginations and tubules, and reducing cytosolic FBP-17 blocked the formation of membrane tubules. Further studies in this system should help to clarify the various stages of clathrin-coated pit formation, invagination, and scission. — SMH

Nat. Cell Biol. **12**, 902 (2010).

CHEMISTRY

Reporting a Break-Up

Phospholipase enzymes play a role in a wide range of physiological processes—including digestion, inflammation response, membrane remodeling, and intercellular signaling—through the degradation of phospholipids. The A₂ class of phospholipases (PLA₂) acts on

glycerophospholipids to produce free fatty acids and lysolipids. As dysregulation of PLA₂ figures in many pathological conditions, measurement of its activity and concentration is important. PLA₂ activity has been shown to be sensitive to environment though, so mounting colorimetric probes on a substrate does not provide accurate measures. Aili *et al.* skirted this problem through the use of a pair of complementary polypeptides, JR2EC and JR2KC. A cysteine residue in the central loop of JR2EC bound the peptide to a gold nanoparticle, whereas the cysteines in two JR2KC chains were covalently linked via a disulfide bridge to form a bifunctional dimer (JR2KC₂). The JR2KC₂ was then loaded into liposomes that were designed to be susceptible to PLA₂ degradation. Once released, the JR2KC₂ tended to hetero-associate with the gold-bonded JR2EC, causing aggregation of the gold nanoparticles and a corresponding red shift of the surface plasmon resonance visible to the naked eye. A lag in the detection time could be correlated with the concentration of PLA₂ over a sensitivity range spanning 7 nM to 700 pM. — MSL

Nano Lett. **10**, 10.1021/nl1024062 (2010).

PSYCHOLOGY

True Insights from False Memories

Archimedes is reputed to have solved the problem of determining whether silver had been substituted for gold in a votive crown after a flash of insight as he bathed. Suppose, however, that instead of stepping into a full bathtub, he had been asked by his local psychologist to recall words from a list that he had just heard—a list that did not contain the word “water” but did contain words such as bath, wash, and tub. Would Archimedes have still have cried, “Eureka!”? Howe *et al.* show that he very probably would have. They demonstrate that using the classical Deese/Roediger-McDermott paradigm to prime a false memory that a target word is on a list of topically related words enabled people to answer more accurately and rapidly when challenged on compound remote associate tasks where the target word was the correct answer. An example of such a task would be to come up with the word “water” when presented with the three words sea, melon, and skiing. Furthermore, this performance increment was observed even when people were simply exposed to the lists, indicating that the automatic generation of the false memory, which is thought to occur during encoding of the list, was sufficient to improve problem solving. — GJC

Cognition **117**, 10.1016/j.cognition.2010.08.009 (2010).

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