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**RESEARCH ARTICLE: Poverty Impedes Cognitive Function**

**Abstract:** The poor often behave in less capable ways, which can further perpetuate poverty. We hypothesize that poverty directly impedes cognitive function and present two studies that test this hypothesis. First, we experimentally induced thoughts about finances and found that this reduces cognitive performance among poor but not in well-off participants. Second, we examined the cognitive function of farmers over the planting cycle. We found that the same farmer shows diminished cognitive performance before harvest, when poor, as compared with after harvest, when rich. This cannot be explained by differences in time available, nutrition, or work effort. Nor can it be explained with stress: Although farmers do show more stress before harvest, that does not account for diminished cognitive performance. Instead, it appears that poverty itself reduces cognitive capacity. We suggest that this is because poverty-related concerns consume mental resources, leaving less for other tasks. These data provide a previously unexamined perspective and help explain a spectrum of behaviors among the poor. We discuss some implications for poverty policy.

[Supporting online material](#)

**REPORT: Dissecting X-ray–Emitting Gas Around the Center of Our Galaxy**

**Summary:** Most supermassive black holes (SMBHs) are accreting at very low levels and are difficult to distinguish from the galaxy centers where they reside. Our own Galaxy’s SMBH provides an instructive exception, and we present a close-up view of its quiescent x-ray emission based on 3 megaseconds of Chandra observations. Although the x-ray emission is elongated and aligns well with
a surrounding disk of massive stars, we can rule out a concentration of low-mass coronally active stars as the origin of the emission on the basis of the lack of predicted iron (Fe) Kα emission. The extremely weak hydrogen (H)–like Fe Kα line further suggests the presence of an outflow from the accretion flow onto the SMBH. These results provide important constraints for models of the prevalent radiatively inefficient accretion state.

Supporting online material

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**REPORT: Paleofluvial Mega-Canyon Beneath the Central Greenland Ice Sheet**

**Abstract:** Subglacial topography plays an important role in modulating the distribution and flow of basal water. Where topography predates ice sheet inception, it can also reveal insights into former tectonic and geomorphological processes. Although such associations are known in Antarctica, little consideration has been given to them in Greenland, partly because much of the ice sheet bed is thought to be relatively flat and smooth. Here, we present evidence from ice-penetrating radar data for a 750-km-long subglacial canyon in northern Greenland that is likely to have influenced basal water flow from the ice sheet interior to the margin. We suggest that the mega-canyon predates ice sheet inception and will have influenced basal hydrology in Greenland over past glacial cycles.

Supporting online material

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**NEWS & ANALYSIS: Evolution Heresy? Epigenetics Underlies Heritable Plant Traits**

**Summary:** For some evolutionary biologists, just hearing the term epigenetics raises hackles. They balk at suggestions that something other than changes in DNA sequences, such as the chemical addition of methyl groups to DNA or other so-called epigenetic modifications, has a role in evolution. Yet a provocative study presented at an evolutionary biology meeting last month found that heritable changes in plant flowering time and other traits were the result of epigenetics alone, unaided by any sequence changes.
RESEARCH ARTICLE: Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice

Abstract: Establishing whether specific structural and functional configurations of a human gut microbiota are causally related to a given physiologic or disease phenotype is challenging. Twins discordant for obesity provide an opportunity to examine interrelations between obesity and its associated metabolic disorders, diet, and the gut microbiota. Transplanting the intact uncultured or cultured human fecal microbiota from each member of a discordant twin pair into separate groups of recipient germfree mice permits the donors’ communities to be replicated, differences between their properties to be identified, the impact of these differences on body composition and metabolic phenotypes to be discerned, and the effects of diet-by-microbiota interactions to be analyzed. In addition, cohousing coprophagic mice harboring transplanted microbiota from discordant pairs provides an opportunity to determine which bacterial taxa invade the gut communities of cage mates, how invasion correlates with host phenotypes, and how invasion and microbial niche are affected by human diets.

Supporting online material

PERSPECTIVE: Fighting Obesity with Bacteria

Summary: The human large intestine harbors a complex community of microorganisms (microbiota) that affect many aspects of our physiology and health (1). Numerous lines of evidence, particularly from rodent models, have suggested that the intestinal microbiota may play a role in the development of obesity. On page 1241214 of the September 6, 2013 issue of Science, Ridaura et al. (2) demonstrate that the microbiota from lean or obese humans induces similar phenotypes in mice and, more remarkably, that the microbiota from lean donors can invade and reduce adiposity gain in the obese-recipient mice if the mice are fed an appropriate diet.

REPORT: Interacting Gears Synchronize Propulsive Leg Movements in a Jumping Insect

Abstract: Gears are found rarely in animals and have never been reported to intermesh and rotate functionally like mechanical gears. We now demonstrate functional gears in the ballistic jumping movements of the flightless planthopper insect Issus. The nymphs, but not adults, have a row of cuticular gear (cog) teeth around the curved medial surfaces of their two hindleg trochantera. The gear teeth on one trochanter engaged with and sequentially moved past those on the other trochanter during the preparatory cocking and the propulsive phases of jumping. Close registration between the gears ensured that both hindlegs moved at the same angular velocities to propel the body without yaw rotation. At the final molt to adulthood, this synchronization mechanism is jettisoned.

Supporting online material

NEWS & ANALYSIS: It’s Official—Voyager Has Left the Solar System

Summary: After 36 years of hurtling toward the edge of the solar system, the Voyager 1 spacecraft—its sensors failing, its energy running low—has crossed into the abyss of interstellar space. At least, after long disagreements, that is now the consensus view of Voyager mission team
leaders. The space physicists' edge of the solar system "is not your usual planetary environment at all," says heliophysicist George Gloeckler, a Voyager team member since the 1960s. Even modern computer simulations could give no warning of the confusing weirdness Voyager 1 has encountered.

Podcast Interview

NEWS FOCUS: A Once-in-a-Lifetime Flu Shot?

Summary: Researchers long have dreamed of a "universal" vaccine that could thwart all strains of the influenza virus and mean goodbye to annual shots and pandemics. But few clues have suggested ways to make this vaccine, as antibodies against the virus tend to work against one strain but not another. New insights about antibodies that have a "broad" reach and stop many, if not all, viral variants may hold answers.


Abstract: Soluble β-amyloid (Aβ) oligomers impair synaptic plasticity and cause synaptic loss associated with Alzheimer’s disease (AD). We report that murine PirB (paired immunoglobulin-like receptor B) and its human ortholog LilrB2 (leukocyte immunoglobulin-like receptor B2), present in human brain, are receptors for Aβ oligomers, with nanomolar affinity. The first two extracellular immunoglobulin (Ig) domains of PirB and LilrB2 mediate this interaction, leading to enhanced cofilin signaling, also seen in human AD brains. In mice, the deleterious effect of Aβ oligomers on hippocampal long-term potentiation required PirB, and in a transgenic model of AD, PirB not only contributed to memory deficits present in adult mice, but also mediated loss of synaptic plasticity in juvenile visual cortex. These findings imply that LilrB2 contributes to human AD neuropathology and suggest therapeutic uses of blocking LilrB2 function.

Supporting online material

NEWS & ANALYSIS: Secretive and Subjective, Peer Review Proves Resistant to Study

Summary: At the International Congress on Peer Review and Biomedical Publication, efforts to explore the scientific literature have shifted away from peer review and into other areas, such as bias and authorship. With a dearth of available data and funding, large systematic studies of how peer review works and doesn't aren't easy to get off the ground.

REPORT: Linear Structures in the Core of the Coma Cluster of Galaxies

Abstract: The hot x-ray–emitting plasma in galaxy clusters is predicted to have turbulent motion, which can contribute around 10% of the cluster’s central energy density. We report deep Chandra X-ray Observatory observations of the Coma cluster core, showing the presence of quasi-linear high-density arms spanning 150 kiloparsecs, consisting of low-entropy material that was probably stripped from merging subclusters. Two appear to be connected with a subgroup of galaxies at a 650-kiloparsec radius that is merging into the cluster, implying coherence over several hundred million years. Such a long lifetime implies that strong isotropic turbulence and conduction are suppressed in the core, despite the unrelaxed state of the cluster. Magnetic fields are presumably responsible. The structures seen in Coma present insight into the past billion years of subcluster merger activity.

Supporting online material
RESEARCH ARTICLE: Maternal Hyperglycemia Activates an ASK1–FoxO3a–Caspase 8 Pathway That Leads to Embryonic Neural Tube Defects

Abstract: Neural tube defects result from failure to completely close neural tubes during development. Maternal diabetes is a substantial risk factor for neural tube defects, and available evidence suggests that the mechanism that links hyperglycemia to neural tube defects involves oxidative stress and apoptosis. We demonstrated that maternal hyperglycemia correlated with activation of the apoptosis signal–regulating kinase 1 (ASK1) in the developing neural tube, and Ask1 gene deletion was associated with reduced neuroepithelial cell apoptosis and development of neural tube defects. ASK1 activation stimulated the activity of the transcription factor FoxO3a, which increased the abundance of the apoptosis-promoting adaptor protein TRADD, leading to activation of caspase 8. Hyperglycemia-induced apoptosis and the development of neural tube defects were reduced with genetic ablation of either FoxO3a or Casp8 or inhibition of ASK1 by thioredoxin. Examination of human neural tissues affected by neural tube defects revealed increased activation or abundance of ASK1, FoxO3a, TRADD, and caspase 8. Thus, activation of an ASK1–FoxO3a–TRADD–caspase 8 pathway participates in the development of neural tube defects, which could be prevented by inhibiting intermediates in this cascade.

Supplementary Materials

RESEARCH ARTICLE: The Endoplasmic Reticulum Acts as a Platform for Ubiquitylated Components of Nuclear Factor κB Signaling

Abstract: The innate and adaptive immune responses involve the stimulation of nuclear factor κB (NF-κB) transcription factors through the Lys^63 (K^63)–linked ubiquitylation of specific components of NF-κB signaling pathways. We found that ubiquitylated components of the NF-κB pathway accumulated on the cytosolic leaflet of the endoplasmic reticulum (ER) membrane after the engagement of cell-surface, proinflammatory cytokine receptors or antigen receptors. Through mass spectrometric analysis, we found that the ER-anchored protein metadherin (MTDH) was a partner for these ubiquitylated activators of NF-κB and that it directly bound to K^63-linked polyubiquitin chains. Knockdown of MTDH inhibited the accumulation of ubiquitylated NF-κB signaling components at the ER, reduced the extent of NF-κB activation, and decreased the amount of proinflammatory cytokines produced. Our observations highlight an unexpected facet of the ER as a key subcellular gateway for NF-κB activation.

Supplementary Materials

RESEARCH ARTICLE: Ajuba Family Proteins Link JNK to Hippo Signaling

Abstract: Wounding, apoptosis, or infection can trigger a proliferative response in neighboring cells to replace damaged tissue. Studies in Drosophila have implicated c-Jun amino-terminal kinase (JNK)–dependent activation of Yorkie (Yki) as essential to regeneration-associated growth, as well as growth associated with neoplastic tumors. Yki is a transcriptional coactivator that is inhibited by Hippo signaling, a conserved pathway that regulates growth. We identified a conserved mechanism by which JNK regulated Hippo signaling. Genetic studies in Drosophila identified Jub (also known as Ajuba LIM protein) as required for JNK-mediated activation of Yki and showed that Jub contributed to wing regeneration after wounding and to tumor growth. Biochemical studies revealed that JNK promoted the phosphorylation of Ajuba family proteins in both Drosophila and mammalian cells. Binding studies in mammalian cells indicated that JNK increased binding between the Ajuba family proteins LIMD1 or WTIP and LATS1, a kinase within the Hippo pathway that inhibits the Yki homolog.
YAP. Moreover, JNK promoted binding of LIMD1 and LATS1 through direct phosphorylation of LIMD1. These results identify Ajuba family proteins as a conserved link between JNK and Hippo signaling, and imply that JNK increases Yki and YAP activity by promoting the binding of Ajuba family proteins to Warts and LATS.

**RESEARCH ARTICLE: A Cancer-Associated Mutation in Atypical Protein Kinase C(iota) Occurs in a Substrate-Specific Recruitment Motif**

**Abstract:** Atypical protein kinase Ci(PKCi) has roles in cell growth, cellular polarity, and migration, and its abundance is frequently increased in cancer. We identified a protein interaction surface containing a dibasic motif (RIPR) that bound a distinct subset of PKCi substrates including lethal giant larvae 2 (LLGL2) and myosin X, but not other substrates such as Par3. Further characterization demonstrated that Arg471 in this motif was important for binding to LLGL2, whereas Arg474 was critical for interaction with myosin X, indicating that multiple complexes could be formed through this motif. A somatic mutation of the dibasic motif (R471C) was the most frequent mutation of PKCi in human cancer, and the intact dibasic motif was required for normal polarized epithelial morphogenesis in three-dimensional cysts. Thus, the R471C substitution is a change-of-function mutation acting at this substrate-specific recruitment site to selectively disrupt the polarizing activity of PKCi.

**Supplementary Materials**

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**In Science Translational Medicine**

**RESEARCH ARTICLE: Molecular Mechanism for Age-Related Memory Loss: The Histone-Binding Protein RbAp48**

**Abstract:** To distinguish age-related memory loss more explicitly from Alzheimer’s disease (AD), we have explored its molecular underpinning in the dentate gyrus (DG), a subregion of the hippocampal formation thought to be targeted by aging. We carried out a gene expression study in human postmortem tissue harvested from both DG and entorhinal cortex (EC), a neighboring subregion unaffected by aging and known to be the site of onset of AD. Using expression in the EC for normalization, we identified 17 genes that manifested reliable age-related changes in the DG. The most significant change was an age-related decline in RbAp48, a histone-binding protein that modifies histone acetylation. To test whether the RbAp48 decline could be responsible for age-related memory loss, we turned to mice and found that, consistent with humans, RbAp48 was less abundant in the DG of old than in young mice. We next generated a transgenic mouse that expressed a dominant-negative inhibitor of RbAp48 in the adult forebrain. Inhibition of RbAp48 in young mice caused hippocampus-dependent memory deficits similar to those associated with aging, as measured by novel object recognition and Morris water maze tests. Functional magnetic resonance imaging studies showed that within the hippocampal formation, dysfunction was selectively observed in the DG, and this corresponded to a regionally selective decrease in histone acetylation. Up-regulation of RbAp48 in the DG of aged wild-type mice ameliorated age-related hippocampus-based memory loss and age-related abnormalities in histone acetylation. Together, these findings show that the DG is a hippocampal subregion targeted by aging, and identify molecular mechanisms of cognitive aging that could serve as valid targets for therapeutic intervention.

**Supplementary material**

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**RESEARCH ARTICLE: Rapid, Label-Free Detection of Brain Tumors with Stimulated Raman Scattering Microscopy**
Abstract: Surgery is an essential component in the treatment of brain tumors. However, delineating tumor from normal brain remains a major challenge. We describe the use of stimulated Raman scattering (SRS) microscopy for differentiating healthy human and mouse brain tissue from tumor-infiltrated brain based on histoarchitectural and biochemical differences. Unlike traditional histopathology, SRS is a label-free technique that can be rapidly performed in situ. SRS microscopy was able to differentiate tumor from nonneoplastic tissue in an infiltrative human glioblastoma xenograft mouse model based on their different Raman spectra. We further demonstrated a correlation between SRS and hematoxylin and eosin microscopy for detection of glioma infiltration (κ = 0.98). Finally, we applied SRS microscopy in vivo in mice during surgery to reveal tumor margins that were undetectable under standard operative conditions. By providing rapid intraoperative assessment of brain tissue, SRS microscopy may ultimately improve the safety and accuracy of surgeries where tumor boundaries are visually indistinct.

Supplementary material

RESEARCH ARTICLE: A Molecular Signature Predictive of Indolent Prostate Cancer

Abstract: Many newly diagnosed prostate cancers present as low Gleason score tumors that require no treatment intervention. Distinguishing the many indolent tumors from the minority of lethal ones remains a major clinical challenge. We now show that low Gleason score prostate tumors can be distinguished as indolent and aggressive subgroups on the basis of their expression of genes associated with aging and senescence. Using gene set enrichment analysis, we identified a 19-gene signature enriched in indolent prostate tumors. We then further classified this signature with a decision tree learning model to identify three genes—FGFR1, PMP22, and CDKN1A—that together accurately predicted outcome of low Gleason score tumors. Validation of this three-gene panel on independent cohorts confirmed its independent prognostic value as well as its ability to improve prognosis with currently used clinical nomograms. Furthermore, protein expression of this three-gene panel in biopsy samples distinguished Gleason 6 patients who failed surveillance over a 10-year period. We propose that this signature may be incorporated into prognostic assays for monitoring patients on active surveillance to facilitate appropriate courses of treatment.

Supplementary material

RESEARCH ARTICLE: A Host-Based RT-PCR Gene Expression Signature to Identify Acute Respiratory Viral Infection

Abstract: Improved ways to diagnose acute respiratory viral infections could decrease inappropriate antibacterial use and serve as a vital triage mechanism in the event of a potential viral pandemic. Measurement of the host response to infection is an alternative to pathogen-based diagnostic testing and may improve diagnostic accuracy. We have developed a host-based assay with a reverse transcription polymerase chain reaction (RT-PCR) TaqMan low-density array (TLDA) platform for classifying respiratory viral infection. We developed the assay using two cohorts experimentally infected with influenza A H3N2/Wisconsin or influenza A H1N1/Brisbane, and validated the assay in a sample of adults presenting to the emergency department with fever (n = 102) and in healthy volunteers (n = 41). Peripheral blood RNA samples were obtained from individuals who underwent experimental viral challenge or who presented to the emergency department and had microbiologically proven viral respiratory infection or systemic bacterial infection. The selected gene set on the RT-PCR TLDA assay classified participants with experimentally induced influenza H3N2 and H1N1 infection with 100 and 87% accuracy, respectively. We validated this host gene expression signature in a cohort of 102 individuals arriving at the emergency department. The sensitivity of the RT-PCR test was 89% [95% confidence interval (CI), 72 to 98%], and the specificity was 94% (95% CI, 86 to 99%). These results show that RT-PCR–based detection of a host gene expression signature can classify individuals with respiratory viral infection and sets the stage for prospective evaluation of this diagnostic approach in a clinical setting.

Supplementary material