

***NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH  
(ICMR-NIOH)***

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***December, 2021***

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# American Journal of Epidemiology

Volume 190 Number 12 December 2021

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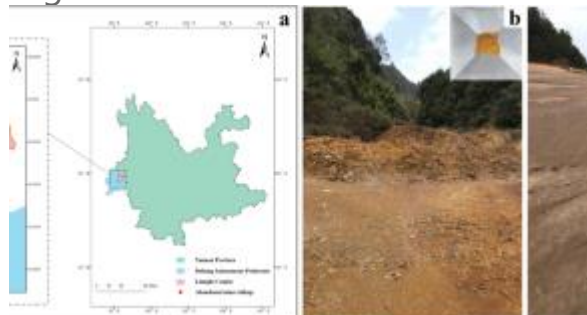
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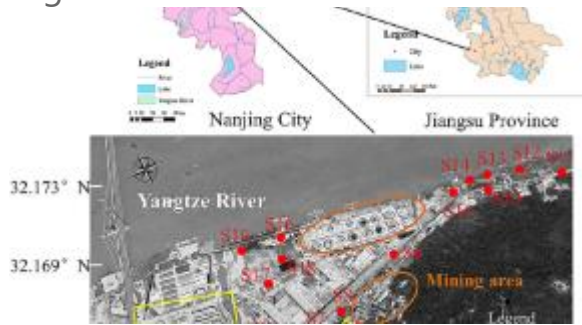
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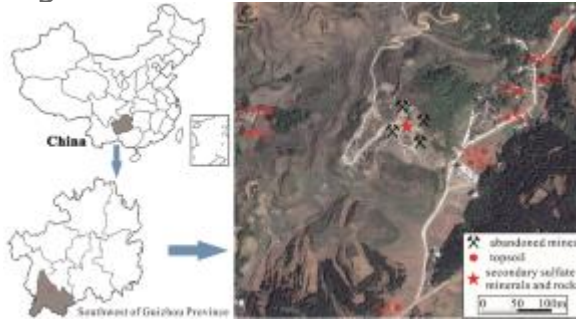
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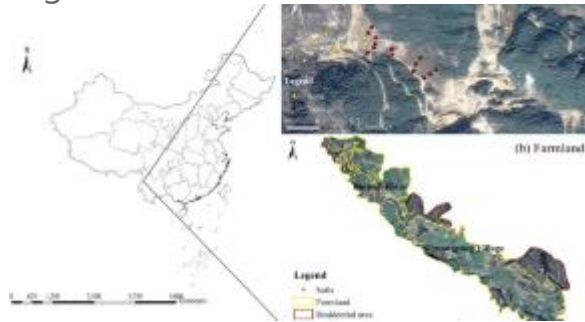
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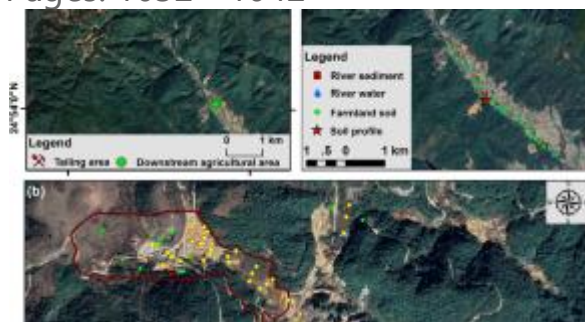
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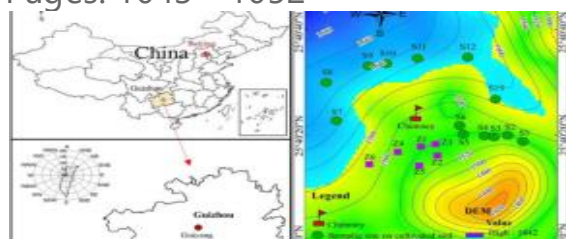
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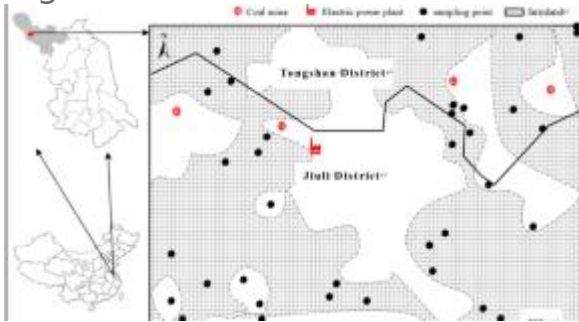
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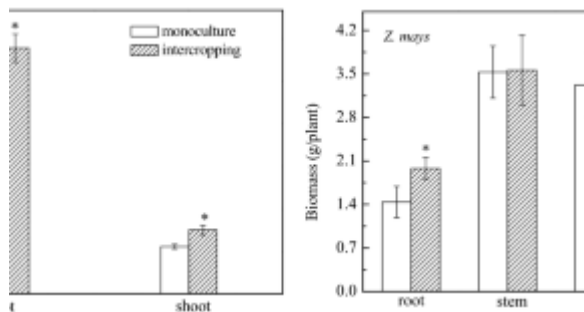
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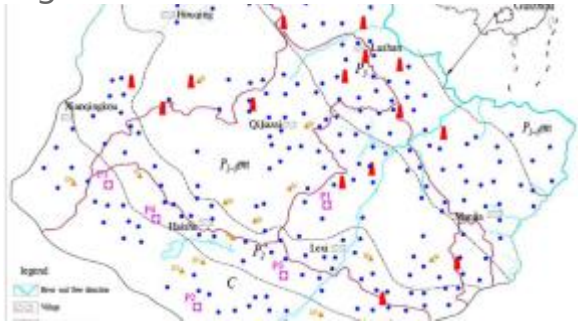
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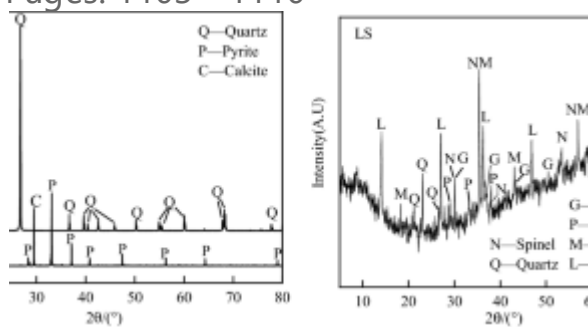
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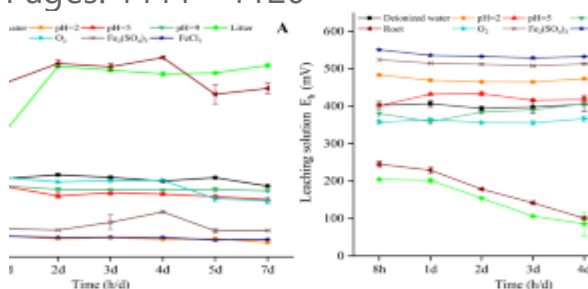
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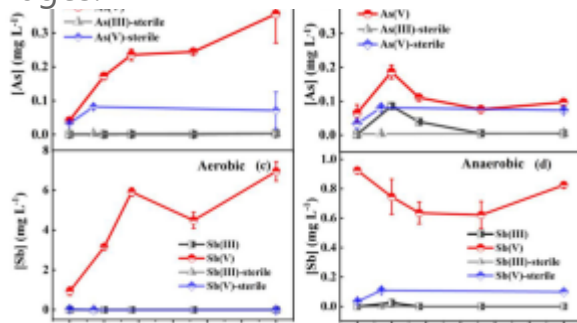
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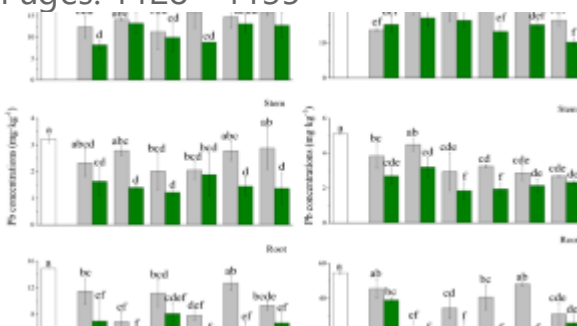
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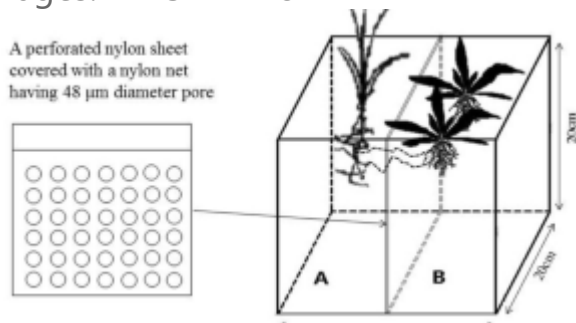
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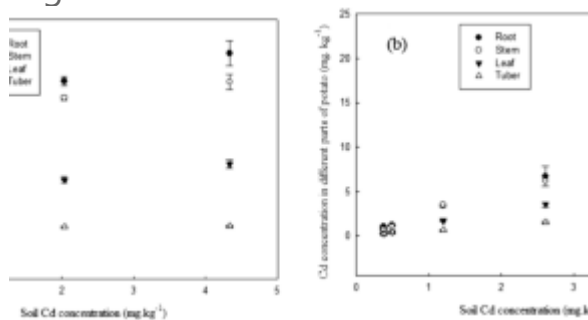
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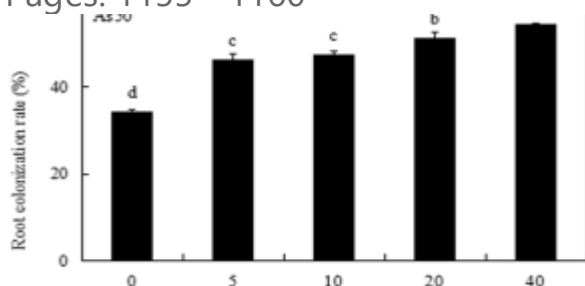
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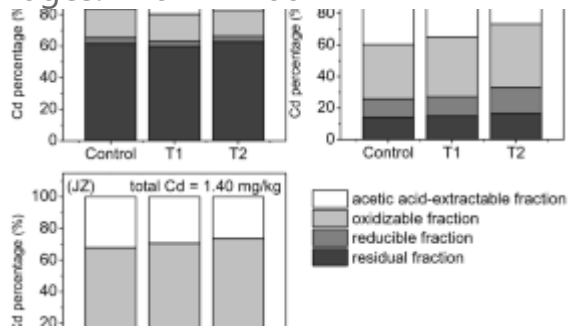
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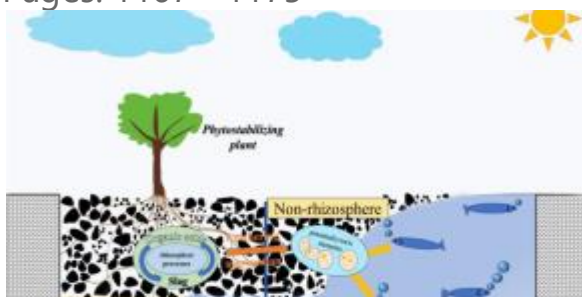
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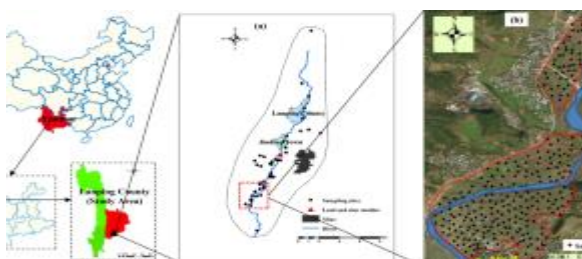
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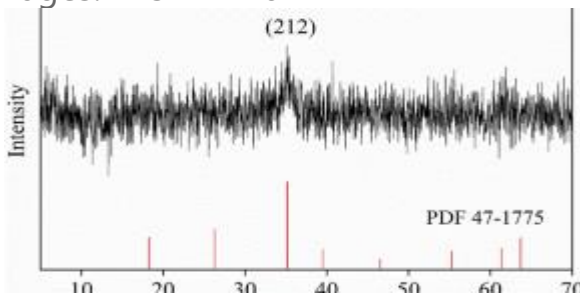
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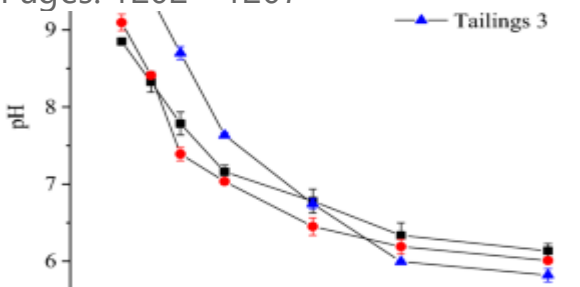
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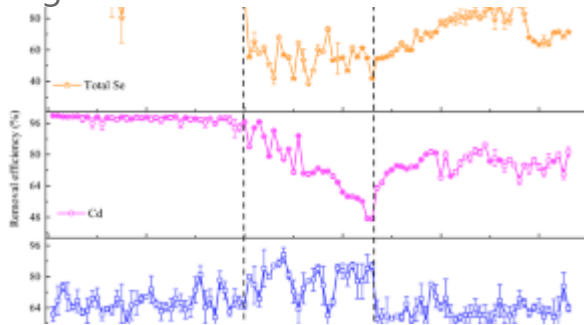
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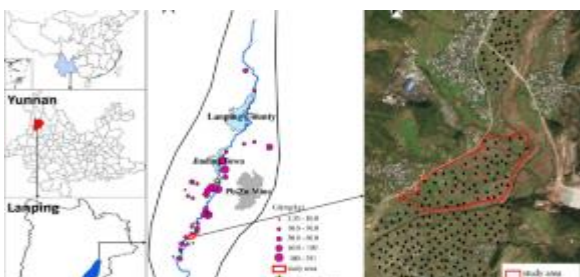
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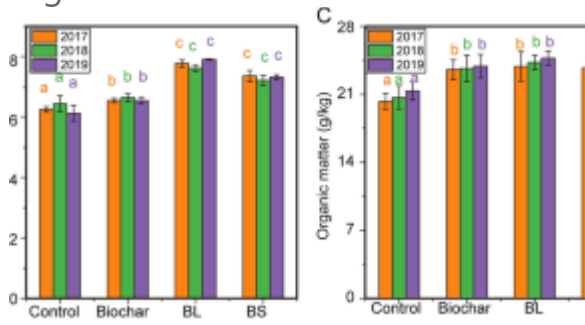
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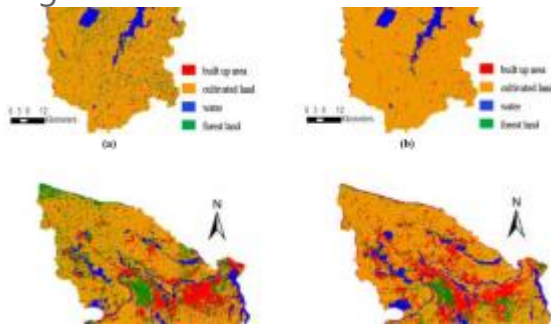
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## Corrigendum

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Bull World Health Organ. 2021 Dec 1; 99(12): 912. Published online 2021 Dec 1. doi: 10.2471/BLT.21.101221

**Corrects:** [Bull World Health Organ. 2021 Nov 1; 99\(11\): 837–839.](#)

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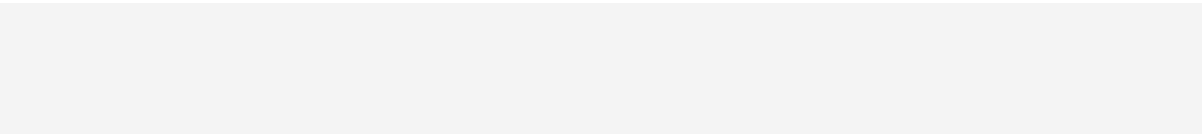
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# Nature

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- Editorial | 01 December 2021  
**Industry scores higher than academia for job satisfaction**  
*Nature's* salary survey finds that industry researchers are more positive about their careers. Academia must raise its game.

### World View

- World View | 29 November 2021  
**Victories against AIDS have lessons for COVID-19**  
Anthony Fauci on four decades of progress against HIV, and what's needed for the future.
  - Anthony Fauci

### Research Highlights

- Research Highlight | 24 November 2021  
**The 3D print job that keeps quake damage at bay**  
An easily produced seismic isolator designed to protect buildings from earthquakes mimics the bones of human limbs.
- Research Highlight | 24 November 2021  
**How jellyfish control their lives**  
Transgenic jellyfish reveal how these fragile creatures get by without a brain.

- Research Highlight | 24 November 2021  
**Hard times tear coupled seabirds apart**  
Even birds get divorced, and, as in humans, resource constraints can drive more couples to the brink.
- Research Highlight | 24 November 2021  
**Tidings from an exploding star make astronomers happy**  
Herculean stellar event provides scientific clues to how stars die.
- Research Highlight | 24 November 2021  
**Neutron beam sheds light on medieval faith and superstition**  
Hidden inside a leaden amulet, researchers find words of magic and Christian creed side by side.
- Research Highlight | 23 November 2021  
**Mini-machine can chop and channel proteins**  
Scientists' creation can cut proteins into pieces and thread them through a molecular tunnel.
- Research Highlight | 23 November 2021  
**Earth is headed for well over two degrees of warming**  
Modellers look at how climate policies might change with time — and find a wide range of possible outcomes, none of them good.

## Research

### News & Views

- News & Views | 01 December 2021  
**Robotic sample return reveals lunar secrets**  
A mission to unexplored lunar territory has returned the youngest volcanic samples collected so far. The rocks highlight the need to make revisions to models of the thermal evolution of the Moon.
  - Richard W. Carlson
- News & Views | 01 November 2021  
**A reconstruction of early cryptic COVID spread**  
To respond better to future pandemics, we must understand how the SARS-CoV-2 virus dispersed so rapidly. A model of COVID-19 spread

sheds light on cryptic transmission, undetected by surveillance efforts, in early 2020.

- Simon Cauchemez
- Paolo Bosetti

- News & Views | 03 November 2021

**A seagrass harbours a nitrogen-fixing bacterial partner**

How underwater seagrasses obtain the nitrogen they need has been unclear. Evidence has now emerged of a partnership with a bacterium that might be analogous to the system used by many land plants to gain nitrogen.

- Douglas G. Capone

- News & Views | 01 December 2021

**Choreographing water molecules to speed up hydrogen production**

A technical feat reveals subtle changes in water structure that can accelerate hydrogen production at an electrode interface. The catalytic process could be developed to help boost supply of this clean fuel.

- Matthias M. Waagele

- News & Views | 01 December 2021

**Artificial intelligence aids intuition in mathematical discovery**

Machine-learning tools have been used to assist the part of mathematical research that usually relies on human intuition and creativity — leading to two fundamental results in different areas of mathematics.

- Christian Stump

- News & Views | 17 November 2021

**Helpline data used to monitor population distress in a pandemic**

The initial stages of the COVID-19 pandemic saw an increase in calls to mental-health helplines in 19 countries. Helpline-call data can be used to monitor distress at a population level in near-real time.

- Cindy H. Liu
- Alexander C. Tsai

## Articles

- Article | 19 October 2021 | Open Access  
**A dry lunar mantle reservoir for young mare basalts of Chang'e-5**  
Water abundance and hydrogen isotope compositions of two-billion-year-old basalt samples returned from the Moon by the Chang'e-5 mission suggest that the samples came from a relatively dry mantle source.
  - Sen Hu
  - Huicun He
  - Ziyuan Ouyang
- Article | 19 October 2021 | Open Access  
**Two-billion-year-old volcanism on the Moon from Chang'e-5 basalts**  
Basalt samples returned from the Moon by the Chang'e-5 mission are revealed to be two billion years old by radioisotopic dating, providing insight on the volcanic history of the Moon.
  - Qiu-Li Li
  - Qin Zhou
  - Xian-Hua Li
- Article | 19 October 2021 | Open Access  
**Non-KREEP origin for Chang'e-5 basalts in the Procellarum KREEP Terrane**  
Isotopic analysis of basalt clasts returned from the Moon by the Chang'e-5 mission indicates that the rocks were derived from a mantle source that lacked potassium, rare-earth elements and phosphorus.
  - Heng-Ci Tian
  - Hao Wang
  - Fu-Yuan Wu
- Article | 01 December 2021  
**Sound emission and annihilations in a programmable quantum vortex collider**  
By controlling the generation and collision of individual vortices in atomic Fermi superfluids, a study provides a comprehensive view of vortex decay due to mutual friction and vortex–sound interaction.
  - W. J. Kwon
  - G. Del Pace
  - G. Roati

- Article | 01 December 2021 | Open Access  
**Advancing mathematics by guiding human intuition with AI**  
 A framework through which machine learning can guide mathematicians in discovering new conjectures and theorems is presented and shown to yield mathematical insight on important open problems in different areas of pure mathematics.
  - Alex Davies
  - Petar Veličković
  - Pushmeet Kohli
  
- Article | 01 December 2021  
**Optomechanical dissipative solitons**  
 Stable, dissipative optomechanical solitons are realized using optical fields in a whispering gallery mode resonator by balancing the optomechanical nonlinearities with a tailored modal dispersion.
  - Jing Zhang
  - Bo Peng
  - Lan Yang
  
- Article | 01 December 2021  
**In situ Raman spectroscopy reveals the structure and dissociation of interfacial water**  
 Interfacial water consists of hydrogen-bonded water and  $\text{Na}\cdot\text{H}_2\text{O}$ , its structure changes at hydrogen evolution reaction (HER) potentials, and when structurally ordered it aids interfacial electron transfer, resulting in higher HER rates.
  - Yao-Hui Wang
  - Shisheng Zheng
  - Jian-Feng Li
  
- Article | 20 October 2021 | Open Access  
**Late Quaternary dynamics of Arctic biota from ancient environmental genomics**  
 A large-scale metagenomic analysis of plant and mammal environmental DNA reveals complex ecological changes across the circumpolar region over the past 50,000 years, as biota responded to changing climates, culminating in the postglacial extinction of large mammals and emergence of modern ecosystems.
  - Yucheng Wang
  - Mikkel Winther Pedersen
  - Eske Willerslev

- Article | 10 November 2021  
**Temporal transitions in the post-mitotic nervous system of *Caenorhabditis elegans***  
 In the post-mitotic nervous system of *Caenorhabditis elegans*, the promotion of a mature neuronal transcription program is controlled by the developmental-stage-specific upregulation of the microRNA LIN-4 and the subsequent repression of its target, the transcription factor *lin-14*.
  - HaoSheng Sun
  - Oliver Hobert
- Article | 06 October 2021 | Open Access  
**Thalamic circuits for independent control of prefrontal signal and noise**  
 Two different cell types in the mediodorsal thalamus have complementary roles in decision-making, with one type of mediodorsal projection amplifying prefrontal activity under low signal levels and one type suppressing it under high noise levels.
  - Arghya Mukherjee
  - Norman H. Lam
  - Michael M. Halassa
- Article | 03 November 2021 | Open Access  
**Terrestrial-type nitrogen-fixing symbiosis between seagrass and a marine bacterium**  
 The N<sub>2</sub>-fixing symbiont '*Candidatus Celerinatantimonas neptuna*' lives inside the root tissue of the seagrass *Posidonia oceanica*, providing ammonia and amino acids to its host in exchange for sugars and enabling highly productive seagrass meadows to thrive in the nitrogen-limited Mediterranean Sea.
  - Wiebke Mohr
  - Nadine Lehnen
  - Marcel M. M. Kuypers
- Article | 24 November 2021  
**The human microbiome encodes resistance to the antidiabetic drug acarbose**  
 Bacteria in the human gut and oral microbiome encode enzymes that selectively phosphorylate the antidiabetic drug acarbose—an inhibitor of both human and bacterial α-glucosidases—resulting in its inactivation and limiting the drug's effects on the ability of the host to metabolize complex carbohydrates.
  - Jared Balaich



- Michael Estrella
- Mohamed S. Donia
  
- Article | 01 December 2021  
**Antiviral activity of bacterial TIR domains via immune signalling molecules**  
 The mechanism of Thoeris—a bacterial anti-phage defence system—is described in detail, revealing that bacterial TIR-domain proteins recognize infection and produce signalling molecules to execute cell death, akin to the roles of these proteins in plants.
- Gal Ofir
- Ehud Herbst
- Rotem Sorek
  
- Article | 17 November 2021  
**Mental health concerns during the COVID-19 pandemic as revealed by helpline calls**  
 Data collected from crisis helplines during the COVID-19 pandemic show that pandemic-related issues replaced rather than exacerbated underlying anxieties, and demonstrate that helpline data are useful indicators of public mental health.
- Marius Brühlhart
- Valentin Klotzbücher
- Stephanie K. Reich
  
- Article | 25 October 2021 | Open Access  
**Cryptic transmission of SARS-CoV-2 and the first COVID-19 wave**  
 Modelling highlights international travel as the main driver of the introduction of SARS-CoV-2 to Europe and the USA, and suggests that introductions and local transmission may have begun in January 2020.
- Jessica T. Davis
- Matteo Chinazzi
- Alessandro Vespignani
  
- Article | 17 November 2021 | Open Access  
**Independent infections of porcine deltacoronavirus among Haitian children**  
 The presence of porcine deltacoronavirus has been detected in three children from Haiti that could have originated from zoonotic spillover.
- John A. Lednicky
- Massimiliano S. Tagliamonte
- J. Glenn Morris Jr

- Article | 10 November 2021  
**Self-guarding of MORC3 enables virulence factor-triggered immunity**  
MORC3 is revealed as an essential negative regulator of the anti-viral interferon response that functions in an innate immune pathway that detects viral virulence factors.
  - Moritz M. Gaidt
  - Alyssa Morrow
  - Russell E. Vance
- Article | 13 October 2021  
**Structural basis of cytokine-mediated activation of ALK family receptors**  
Structural studies of the complex of anaplastic lymphoma kinase and leukocyte tyrosine kinase and their activating cytokines identify unique architectural features of the complex, and provide a novel mechanistic paradigm among receptor tyrosine kinases.
  - Steven De Munck
  - Mathias Provost
  - Savvas N. Savvides
- Article | 24 November 2021  
**Structural basis for ligand reception by anaplastic lymphoma kinase**  
Analysis of crystal structures of anaplastic lymphoma kinase elucidate the mechanism by which ligand binding and the glycine-rich domain regulate its activity.
  - Tongqing Li
  - Steven E. Stayrook
  - Daryl E. Klein
- Article | 24 November 2021  
**Mechanism for the activation of the anaplastic lymphoma kinase receptor**  
Cryo-electron microscopy, nuclear magnetic resonance and X-ray crystallography are used to provide structural and mechanistic details of the activation of anaplastic lymphoma kinase by the ligands ALKAL1 and ALKAL2.
  - Andrey V. Reshetnyak
  - Paolo Rossi
  - Charalampos G. Kalodimos

- Article | 24 November 2021  
**Aldehyde-driven transcriptional stress triggers an anorexic DNA damage response**  
Endogenous formaldehyde accumulation reveals Cockayne syndrome in mice and stimulates production of the anorexiogenic peptide GDF15 in proximal tubule cells.
  - Lee Mulderrig
  - Juan I. Garaycochea
  - Ketan J. Patel
- Article | 17 November 2021  
**Structure, function and pharmacology of human itch receptor complexes**  
Cryo-electron microscopy structures of the MRGPRX2–G<sub>ii</sub> trimer in complex with polycationic compound 48/80 or inflammatory peptides provide insights into the sensing of cationic allergens by MRGPRX2, potentially facilitating the design of therapies to prevent unwanted pseudoallergic reactions.
  - Fan Yang
  - Lulu Guo
  - Jin-Peng Sun
- Article | 17 November 2021  
**Structure, function and pharmacology of human itch GPCRs**  
Structural studies of the itch receptors MRGPRX2 and MRGPRX4 in complex with endogenous and synthetic ligands provide a basis for the development of therapeutic compounds for pain, itch and mast cell-mediated hypersensitivity.
  - Can Cao
  - Hye Jin Kang
  - Bryan L. Roth

# Volume 600 Issue 7888, 9 December 2021

## This Week

### Editorial

- Editorial | 08 December 2021  
**The UN must get on with appointing its new science board**  
The decision to appoint a board of advisors is welcome — and urgent, given the twin challenges of COVID and climate change.
- Editorial | 07 December 2021  
**Omicron: the global response is making it worse**  
The pandemic will not end while vaccine equity keeps getting pushed to the margins.

### World View

- World View | 06 December 2021  
**Understand the real reasons reproducibility reform fails**  
Lack of rigour is often blamed on pressure to publish. But ethnographers can find out what truly keeps science from upping its game.
  - Nicole C. Nelson

### Research Highlights

- Research Highlight | 02 December 2021  
**Does police outreach cut crime? Efforts in six nations give a bleak answer**  
Community policing in the global south fails to reduce crime rates or public mistrust.
- Research Highlight | 01 December 2021  
**This enormous eagle could have killed you, probably**  
The extinct Haast's eagle — known from fossils found in New Zealand — hunted like its modern relatives, but also had habits of a scavenger.

- Research Highlight | 01 December 2021  
[Shutting 'super-polluters' slashes greenhouse gases — and deaths](#)  
Early retirement for climate-damaging power plants would also cut emissions of air pollution that endanger human health.
- Research Highlight | 02 December 2021  
[Famous space family has a surprisingly peaceful history](#)  
The seven planets orbiting the star TRAPPIST-1 were largely spared cosmic collisions, raising questions about where these worlds got their water.
- Research Highlight | 06 December 2021  
[What fuelled an ancient empire's rise? Potatoes and quinoa](#)  
The Andean superpower Tiwanaku developed with the help of a stable source of nutrients, including llama meat.
- Research Highlight | 30 November 2021  
[Across the Sahara in a day: swifts zip across the desert at amazing rates](#)  
A species of swift lives up to its name as it migrates from southern Europe to central Africa.
- Research Highlight | 06 December 2021  
[Super jelly springs back from a squashing](#)  
This fabricated gel doesn't crack under pressure.

## Research

### News & Views

- News & Views | 17 November 2021  
[A peek into the black box of human embryology](#)  
The molecular mechanisms involved in human gastrulation, a crucial stage in early embryonic development, have been largely elusive. Gene-expression data from a gastrulating human embryo shed light on this process.
  - Alexander Goedel
  - Fredrik Lanner

- News & Views | 08 December 2021  
**Constraints on estimating the CO<sub>2</sub> fertilization effect emerge**  
 Plants offset a large fraction of Earth's carbon dioxide emissions, but estimating the size of this carbon sink relies on differing terrestrial-biosphere models. Combining multiple models with data has now reduced the uncertainty.
  - Chris Huntingford
  - Rebecca J. Oliver
  
- News & Views | 25 October 2021  
**Clues that natural killer cells help to control COVID**  
 Natural killer cells can destroy cells infected by SARS-CoV-2, but this immune-system defence malfunctions in people with severe COVID-19. Will this finding drive a search for ways to reinvigorate natural killer cells in such cases?
  - Emilie Narni-Mancinelli
  - Eric Vivier
  
- News & Views | 08 December 2021  
**Giant planet imaged orbiting two massive stars**  
 Direct imaging has revealed the existence of a large planet orbiting a binary system that contains the most massive planet-hosting stars detected so far. The discovery challenges existing models for how planets and stars form.
  - Kaitlin Kratter
  
- News & Views | 07 December 2021  
**From the archive**  
*Nature's* pages feature changes in the number of topics a science lecturer might cover, and official rules about who can be called a chemist.
  
- News & Views | 17 November 2021  
**Cerebellar neurons that curb food consumption**  
 Artificial activation of neurons identified in a brain region called the cerebellum reduces food intake in mice. The findings could have implications for people with appetite disorders.
  - Richard Simerly
  - Ralph DiLeone

## Articles

- Article | 08 December 2021  
**A wide-orbit giant planet in the high-mass b Centauri binary system**  
A direct imaging study demonstrates the existence of a giant planet in a wide orbit around the high-mass b Centauri binary system, and uses measurements of the orbital properties to discuss its formation mechanism.
  - Markus Janson
  - Raffaele Gratton
  - Joseph C. Carson
- Article | 08 December 2021  
**Giant modulation of optical nonlinearity by Floquet engineering**  
Coherent control and giant modulation of optical nonlinearity in a van der Waals layered magnetic insulator is demonstrated using Floquet engineering.
  - Jun-Yi Shan
  - M. Ye
  - D. Hsieh
- Article | 20 October 2021  
**Evidence for unconventional superconductivity in twisted bilayer graphene**  
A study combining tunnelling and Andreev reflection spectroscopy with a scanning tunnelling microscope provides evidence for unconventional superconductivity in magic-angle twisted bilayer graphene.
  - Myungchul Oh
  - Kevin P. Nuckolls
  - Ali Yazdani
- Article | 08 December 2021  
**High-frequency and intrinsically stretchable polymer diodes**  
A stretchable anode, cathode, semiconductor and current collector have been developed to create stretchable diodes that can operate at megahertz frequencies for use in wirelessly operated, skin-like wearable electronics.
  - Naoji Matsuhisa
  - Simiao Niu
  - Zhenan Bao

- Article | 08 December 2021  
**A constraint on historic growth in global photosynthesis due to increasing CO<sub>2</sub>**  
 An emergent constraint combining biosphere models and carbon budget estimates suggests that the increase in the global terrestrial carbon sink is caused largely by a CO<sub>2</sub>-induced increase in photosynthesis.
  - T. F. Keenan
  - X. Luo
  - S. Zhou
  
- Article | 01 December 2021  
**Bizarre tail weaponry in a transitional ankylosaur from subantarctic Chile**  
*Stegouros elengassen*, an ankylosaur from the late Cretaceous of Chile, has a large tail weapon, named a macuahuitl after the Aztec club, with a frond-like structure formed by seven pairs of laterally projecting osteoderms encasing the distal half of the tail.
  - Sergio Soto-Acuña
  - Alexander O. Vargas
  - David Rubilar-Rogers
  
- Article | 01 December 2021  
**Quantifying social organization and political polarization in online platforms**  
 A new method quantifies the social makeup of online communities, and applying it to 14 years of commenting patterns on Reddit shows increased polarization in 2016, driven by new users to the platform.
  - Isaac Waller
  - Ashton Anderson
  
- Article | 17 November 2021  
**Reverse-translational identification of a cerebellar satiation network**  
 Activity in anterior deep cerebellar nuclei reduces food consumption in mice without reducing metabolic rate, potentially identifying a therapeutic target for disorders involving excessive eating.
  - Aloysius Y. T. Low
  - Nitsan Goldstein
  - J. Nicholas Betley
  
- Article | 10 November 2021  
**Allometric rules for mammalian cortical layer 5 neuron biophysics**  
 Analyses of layer 5 cortical pyramidal neurons in 10 mammalian species show that human neurons are distinct in that they do not



follow the expected allometric relationship between neuron size and membrane conductance.

- Lou Beaulieu-Laroche
- Norma J. Brown
- Mark T. Harnett

- Article | 26 November 2021

**Multiview confocal super-resolution microscopy**

A combination of multiview imaging, structured illumination, reconstruction algorithms and deep-learning predictions realizes spatial- and temporal-resolution improvements in fluorescence microscopy to produce super-resolution images from diffraction-limited input images.

- Yicong Wu
- Xiaofei Han
- Hari Shroff

- Article | 17 November 2021

**Single-cell transcriptomic characterization of a gastrulating human embryo**

The single-cell transcriptional profile of a human embryo between 16 and 19 days after fertilization reveals parallels and differences in gastrulation in humans as compared with mouse and non-human primate models.

- Richard C. V. Tyser
- Elmir Mahammadov
- Shankar Srinivas

- Article | 17 November 2021

**Observation of universal ageing dynamics in antibiotic persistence**

Characterizations of bacteria under acute stress reveal features that can be predicted using a conceptual model of physical ageing.

- Yoav Kaplan
- Shaked Reich
- Nathalie Q. Balaban

- Article | 25 October 2021

**Untimely TGF $\beta$  responses in COVID-19 limit antiviral functions of NK cells**

The improper timing of transforming growth factor- $\beta$  production is a hallmark of severe COVID-19 that may impede natural killer cell function and early control of infection.

- Mario Witkowski
- Caroline Tizian

- Andreas Diefenbach
- Article | 10 November 2021  
**Host immunomodulatory lipids created by symbionts from dietary amino acids**  
 The symbiotic gut bacterium *Bacteroides fragilis* produces unique  $\alpha$ -galactosylceramides from host dietary branched-chain amino acids, which are presented as CD1d ligands and immunomodulate natural killer T cells.
  - Sungwhan F. Oh
  - T. Praveena
  - Dennis L. Kasper
- Article | 18 November 2021  
**CRISPR screens unveil signal hubs for nutrient licensing of T cell immunity**  
 CRISPR screening and protein–protein interaction networks identify components and mechanisms of nutrient-dependent mTORC1 signalling in regulatory T cells and reveal how mTORC1 integrates immunological cues and nutrient signals for adaptive immunity.
  - Lingyun Long
  - Jun Wei
  - Hongbo Chi
- Article | 24 November 2021  
**IL-27 signalling promotes adipocyte thermogenesis and energy expenditure**  
 Therapeutic administration of IL-27—serum levels of which are decreased in individuals with obesity—improves thermogenesis, protects against diet-induced obesity and ameliorates insulin resistance in mouse models of obesity.
  - Qian Wang
  - Dehai Li
  - Zhinan Yin
- Article | 24 November 2021  
**The CLIP1-LTK fusion is an oncogenic driver in non-small-cell lung cancer**  
 Whole-transcriptome sequencing of a subset of 75 non-small-cell lung cancer specimens in a multi-institutional genome screening study identified a fusion of the *CLIP1* and *LTK* genes with transformational potential due to constitutive LTK kinase activity.
  - Hiroki Izumi
  - Shingo Matsumoto
  - Koichi Goto

- Article | 24 November 2021  
**FAM72A antagonizes UNG2 to promote mutagenic repair during antibody maturation**  
 FAM72A differentially controls mutation rates by regulating uracil processing at different stages of the cell cycle, thereby regulating somatic hypermutation and class-switch recombination in B cells.
  - Yuqing Feng
  - Conglei Li
  - Alberto Martin
  
- Article | 24 November 2021  
**Fam72a enforces error-prone DNA repair during antibody diversification**  
 FAM72A interacts with UNG2 to regulate the balance between error-prone and error-free DNA repair.
  - Mélanie Rogier
  - Jacques Moritz
  - Bernardo Reina-San-Martin
  
- Article | 17 November 2021  
**Structural insights into Ubr1-mediated N-degron polyubiquitination**  
 Structures of Ubr1 in complex with Ubc2, ubiquitin and two N-degron peptides reveal a Ubc2-binding region and an acceptor ubiquitin-binding loop on Ubr1, providing mechanistic insights into the initiation and elongation steps of ubiquitination catalysed by Ubr1.
  - Man Pan
  - Qingyun Zheng
  - Minglei Zhao
  
- Article | 10 November 2021  
**Structures of the HER2–HER3–NRG1 $\beta$  complex reveal a dynamic dimer interface**  
 Cryo-electron microscopy structures of the HER2–HER3–NRG1 $\beta$  complex reveal a dynamic HER2–HER3 interface and explain the mechanism for the activating HER2 cancer mutations.
  - Devan Diwanji
  - Raphael Trenker
  - Natalia Jura

## Volume 600 Issue 7889, 16 December 2021

### This Week

#### Editorial

- Editorial | 15 December 2021  
**Replicating scientific results is tough — but essential**  
A high-profile replication study in cancer biology has obtained disappointing results. Scientists must redouble their efforts to find out why.
- Editorial | 14 December 2021  
**Gender balance at Nature Conferences: an update**  
*Nature* has made progress in improving the representation and participation of women at scientific conferences — but there is still much more to do.

#### World View

- World View | 14 December 2021  
**India — stop looking down on international collaborations**  
Publications co-authored by scientists from the West are sometimes discounted by grant and hiring committees. That needs to change.
  - Arun Kumar Shukla

#### Research Highlights

- Research Highlight | 02 December 2021  
**Surging plastic use is fed by coal power — with deadly results**  
Coal-fired power plants are satisfying the world's voracious appetite for plastic, but their emissions are causing a wave of disease and deaths.
- Research Highlight | 09 December 2021  
**Nervous stomach: lab-grown organs clench like the real thing**  
The most complex stomach organoids yet are made with cells from three layers found in developing embryos.

- Research Highlight | 09 December 2021  
**Why cannabis reeks of skunk**  
Scientists discover sulfurous compounds that help to give pot a rank odour, holding out the promise of fragrance-free bud.
- Research Highlight | 09 December 2021  
**Snake escape: imported reptiles gobble an island's lizards**  
King snakes brought to Gran Canaria have multiplied, wreaking havoc on all of its native reptiles.
- Research Highlight | 08 December 2021  
**'Sky river' brought Iran deadly floods — but also welcome water**  
Moisture from the Mediterranean and Red seas helped to recharge an Iranian lake whose area has shrunk by 90% in recent decades.
- Research Highlight | 07 December 2021  
**It's alive! Bio-bricks can signal to others of their kind**  
Large structures can be built from a microbial material with self-healing properties.
- Research Highlight | 09 December 2021  
**Running of the bulls tramples the laws of crowd dynamics**  
The physics of crowds fails to describe behaviour of pedestrians at a famed bull-running festival.

## Research

### News & Views

- News & Views | 24 November 2021  
**Context is key for learning motor skills**  
A sophisticated theory for learning motor skills places emphasis on the need for inferring context — drawing conclusions about the structure of the environment — for efficiently storing and expressing motor memories.
  - Anne G. E. Collins
  - Samuel D. McDougale

- News & Views | 01 December 2021  
**Hominin footprints at Laetoli reveal a walk on the wild side**  
 Bipedalism is a defining feature of the human lineage, but not all hominin species walked in the same way. New data from a famous palaeoanthropology site reveal that at least two differently bipedal hominins roamed eastern Africa.
  - Stephanie M. Melillo
  
- News & Views | 08 July 2021  
**Human genetic variants identified that affect COVID susceptibility and severity**  
 An individual's genetics can influence their risk of infection and the severity of disease symptoms. A large international study has identified parts of the human genome that can affect the risk of severe COVID-19.
  - Samira Asgari
  - Lionel A. Pousaz
  
- News & Views | 08 December 2021  
**Benefits of megastudies for testing behavioural interventions**  
 Trials of behavioural interventions are hard to compare, hampering policy decision-making. The effects of more than 50 interventions on exercise behaviour have been compared using an experimental design called a megastudy.
  - Heather Royer

### Reviews

- Review Article | 08 December 2021  
**The emergence, genomic diversity and global spread of SARS-CoV-2**  
 The potential origins and global spread of SARS-CoV-2, the emergence of SARS-CoV-2 variants of concern and the importance of genomic surveillance for the control of the COVID-19 pandemic are discussed.
  - Juan Li
  - Shengjie Lai
  - Weifeng Shi

### Perspective

- Perspective | 15 December 2021

## **Biogeochemical extremes and compound events in the ocean**

High-temperature, high-acidity and low-oxygen extremes may pose a particular threat to marine ecosystems, requiring a major effort to understand them and the ability of marine life to respond to them.

- Nicolas Gruber
- Philip W. Boyd
- Meike Vogt

## **Articles**

- Article | 15 December 2021  
**Sublimation-driven convection in Sputnik Planitia on Pluto**  
A modelling study describing the formation of the polygonal surface structures in Sputnik Planitia on Pluto shows that convection driven by ice sublimation can generate planetary-scale surface patterns.
  - Adrien Morison
  - Stéphane Labrosse
  - Gaël Choblet
- Article | 15 December 2021 | Open Access  
**Direct limits for scalar field dark matter from a gravitational-wave detector**  
Using a gravitational-wave detector to listen for dark matter signatures, a direct search for scalar field dark matter was conducted and new upper limits are set on the coupling constants.
  - Sander M. Vermeulen
  - Philip Relton
  - Holger Wittel
- Article | 15 December 2021  
**Observation of Feshbach resonances between a single ion and ultracold atoms**  
Magnetically tunable interactions between lithium atoms and barium ions are used to demonstrate and probe Feshbach resonances between atoms and ions, which could have applications in the fields of experimental quantum simulation and fundamental physics.
  - Pascal Weckesser
  - Fabian Thielemann
  - Tobias Schaetz
- Article | 15 December 2021  
**Detecting spins by their fluorescence with a microwave photon counter**  
An ensemble of electron spins is detected by their microwave fluorescence using a superconducting single microwave photon

counter, making single-spin electron spin resonance spectroscopy a possible future prospect.

- Emanuele Albertinale
- Léo Balembois
- Emmanuel Flurin
  
- Article | 15 December 2021 | Open Access  
**Fractional Chern insulators in magic-angle twisted bilayer graphene**  
A study using local compressibility measurements reports fractional Chern insulator states at low magnetic field in magic-angle twisted bilayer graphene, and establishes the applied magnetic field as a means to tune the Berry curvature distribution.
- Yonglong Xie
- Andrew T. Pierce
- Amir Yacoby
  
- Article | 15 December 2021 | Open Access  
**Tritiation of aryl thianthrenium salts with a molecular palladium catalyst**  
The isotopic label tritium can be selectively added into aromatic organic compounds by a homogenous hydrogenolysis reaction using aryl thianthrenium salts, tritium gas and a molecular palladium catalyst.
- Da Zhao
- Roland Petzold
- Tobias Ritter
  
- Article | 15 December 2021  
**A large West Antarctic Ice Sheet explains early Neogene sea-level amplitude**  
Variations in Miocene sea level can be explained by a large marine-based West Antarctic Ice Sheet.
- J. W. Marschalek
- L. Zurli
- Zhifang Xiong
  
- Article | 15 December 2021  
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### **A fatty molecule shows promise for staving off HIV**

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### **Young star's streamer of scorching-hot gas gives astronomers a fiery first**

Eruption from a star called EK Draconis was observed along with a gargantuan stellar explosion.

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### **Lift off! The biggest known flying creature had an explosive launch**

The gigantic flying reptile *Quetzalcoatlus northropi*, which lived in the age of the dinosaurs, could also walk and even run, with the help of 'ski pole' front limbs.

- Research Highlight | 10 December 2021

### **Heatwaves afflict even the far north's icy seas**

Arctic waters have notched a growing number of extreme events called marine heatwaves, raising fears for the region's more heat-sensitive sea creatures.

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### **Why the 'wobbly bridge' did its infamous shimmy**

Model further challenges the idea that pedestrians walking in step caused the oscillation of London's Millennium Bridge.

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### **How the little finches that amazed Darwin battle a vampire fly**

Mother birds on the Galapagos Islands that hunker down in their nests are the best at warding off the bloodthirsty parasite.

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### **Alternatives to standard quantum theory ruled out**

Standard quantum theory contains square roots of negative numbers. But how essential are these 'imaginary' numbers? A way of disproving analogous theories that omit them has been proposed — and confirmed experimentally.

- William K. Wootters
- News & Views | 15 December 2021

**Stomach cancer gets a triple punch of therapy**

Harnessing immune cells to target tumours is a growing trend. The results of a clinical trial combining such treatment with other standard therapies for gastric cancer have altered medical practice — and more changes are to come.

- Myriam Chalabi
- News & Views | 22 December 2021

**Low-power light modifies electron microscopy**

An optical device designed to control the properties of electron waves inside an electron microscope demonstrates that clever platforms for integrated photonics need not be powered by expensive laser systems.

- Martin Kozák
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**Gut clues to weight gain after quitting smoking**

Research has uncovered factors that underlie the weight gain associated with cessation of smoking. Here, scientists consider the implications of this finding from the perspectives of gut biology and of smoking.

- Matthew P. Spindler
- Jeremiah J. Faith
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**Clever substitutions reveal magnetism in zigzag graphene nanoribbons**

The inclusion of nitrogen atoms stabilizes the zigzag edges of carbon-based nanoribbons, enabling the ribbons to be decoupled from a substrate and providing a probe for their unconventional magnetism.

- Aran Garcia-Lekue
- Daniel Sánchez-Portal
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## What surveys really say

Increasing the sample size of a survey is often thought to increase the accuracy of the results. However, an analysis of big surveys on the uptake of COVID-19 vaccines shows that larger sample sizes do not protect against bias.

- Frauke Kreuter
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- A. J. Castro-Tirado
- N. Østgaard
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### **Quantum theory based on real numbers can be experimentally falsified**

A Bell-like experiment that discriminates between real-number and complex-number multipartite quantum systems could disprove real quantum theory.

- Marc-Olivier Renou
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### **Programmable interactions and emergent geometry in an array of atom clouds**

The reported network of connectivity between atomic ensembles is entirely programmable and independent of its geometrical arrangement, because of the interaction with an optical cavity.

- Avikar Periwal
- Eric S. Cooper



- Monika Schleier-Smith
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**Resonance from antiferromagnetic spin fluctuations for superconductivity in  $UTe_2$**

Inelastic neutron scattering measurements show that superconductivity in  $UTe_2$  is associated with a resonance near antiferromagnetic order that suggests an unexpected spin-singlet component to the electron pairing.

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**Quantum anomalous Hall effect from intertwined moiré bands**

An electric-field-induced topological phase transition from a Mott insulator to a quantum anomalous Hall insulator in near-60-degree-twisted (or AB-stacked)  $MoTe_2/WSe_2$  heterobilayers is reported.

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**Spin splitting of dopant edge state in magnetic zigzag graphene nanoribbons**

Decoupling spin-polarized edge states using substitutional N-atom dopants along the edges of a zigzag graphene nanoribbon (ZGNR) reveals giant spin splitting of a N-dopant edge state, and supports the predicted emergent magnetic order in ZGNRs.

- Raymond E. Blackwell
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- Felix R. Fischer
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**Integrated photonics enables continuous-beam electron phase modulation**

A silicon nitride microresonator is used for coherent phase modulation of a transmission electron microscope beam, with future applications in combining high-resolution microscopy with spectroscopy, holography and metrology.

- Jan-Wilke Henke
- Arslan Sajid Raja

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An electrochemical process stimulates the progression toward the electrode of isolated or 'dead' lithium in a battery, recovering its electrical connection, and the effect is demonstrated by increased cycle life.

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**High-entropy polymer produces a giant electrocaloric effect at low fields**

A study reports and characterizes a high-entropy electrocaloric polymer that switches under low fields, and discusses its potential suitability for use in caloric heat pumps.

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**Rapid microbial methanogenesis during CO<sub>2</sub> storage in hydrocarbon reservoirs**

Microbial methanogenesis converts up to 19% of the carbon dioxide injected into an oil field to methane, suggesting that microbial methanogenesis may be a globally important subsurface process.

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**The power of genetic diversity in genome-wide association studies of lipids**

A genome-wide association meta-analysis study of blood lipid levels in roughly 1.6 million individuals demonstrates the gain of power attained when diverse ancestries are included to improve fine-mapping and polygenic score generation, with gains in locus discovery related to sample size.

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**Cortical responses to touch reflect subcortical integration of LTMR signals**

Genetic manipulation of skin peripheral sensory neurons in mice shows that cortical neuron responses to touch reflect subcortical mixing of signals from both rapidly adapting and slowly adapting low-threshold mechanoreceptors.

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**Mechanical actions of dendritic-spine enlargement on presynaptic exocytosis**

A mechanism of mechanosensation and transduction in the presynaptic boutons is identified, in which sensing of fine pressure leads to enhanced neurotransmitter release.

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**Collective durotaxis along a self-generated stiffness gradient in vivo**

The neural crest of *Xenopus laevis* self-generates a stiffness gradient in the adjacent placodal tissue and follows this gradient by durotaxis.

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**Unrepresentative big surveys significantly overestimated US vaccine uptake**

An analysis of three surveys of COVID-19 vaccine behaviour shows that larger surveys overconfidently overestimated vaccine uptake, a demonstration of how larger sample sizes can paradoxically lead to less accurate estimates.

- Valerie C. Bradley
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### **Immunogenicity and efficacy of heterologous ChAdOx1–BNT162b2 vaccination**

An observational study of more than 13,000 healthcare workers shows that a prime–boost vaccine regimen of AstraZeneca ChAdOx1-S-nCoV-19 with Pfizer BNT162b2 provides enhanced protection against SARS-CoV-2 infection compared with two doses of BNT162b2.

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### **Antigen-presenting innate lymphoid cells orchestrate neuroinflammation**

A subset of inflammatory group 3 innate lymphoid cells, here termed iILC3s, infiltrate the central nervous system and promote neuroinflammation and disease progression in a mouse model of multiple sclerosis.

- John B. Grigg
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### **Gut microbiota modulates weight gain in mice after discontinued smoke exposure**

A study of mice exposed to cigarette smoke suggests that smoking-cessation-induced weight gain is associated with a dysbiotic state that is driven by smoking-related metabolites.

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Interim analysis of a phase III clinical trial of HER2-positive gastric adenocarcinoma shows pembrolizumab plus trastuzumab and chemotherapy improves response rates compared with trastuzumab and chemotherapy alone.

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**ecDNA hubs drive cooperative intermolecular oncogene expression**

Extrachromosomal DNA (ecDNA) congregates in clusters called ecDNA hubs that promote intermolecular interactions between gene-regulatory regions and thereby amplify the expression of oncogenes such as *MYC* in cancer cell lines.

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**A conserved mechanism for regulating replisome disassembly in eukaryotes**

A conserved mechanism for the regulation of replisome disassembly in eukaryotes is shown using cryo-electron microscopy, revealing a role for DNA in the preservation of replisome integrity.

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**Structures of the  $\sigma_2$  receptor enable docking for bioactive ligand discovery**

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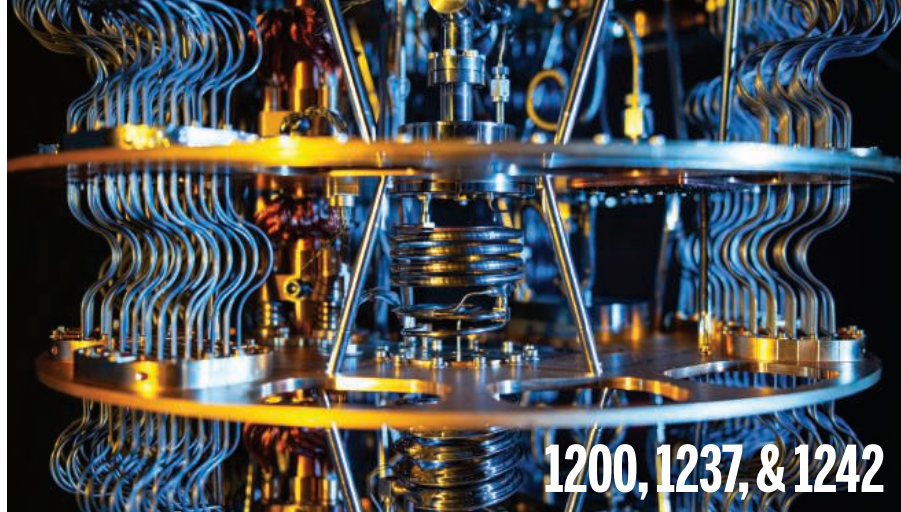
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A stem of the grass *Andropogon gerardii* (also known as “big bluestem”) emerging from a leaf sheath. Grasses, like other monocots, have tall, cylindrical leaves that visually differ from the wide, flat leaves of eudicot plants.

By means of computational modeling and

developmental genetic analysis, researchers have uncovered similarities in the leaf development mechanisms of grasses and eudicot plants. See page 1377. Photo: Bruce Leander/Lady Bird Johnson Wildflower Center



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revealed, are *Science's* 2021 Breakthrough of the Year. *Illustration: V. Altounian/Science; Data: I. R. Humphreys et al., Science 374, eabm4805 (2021); DOI: 10.1126/science.abm4805*

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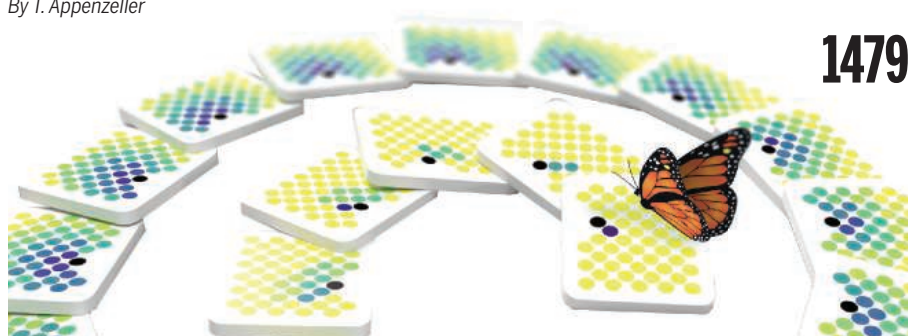
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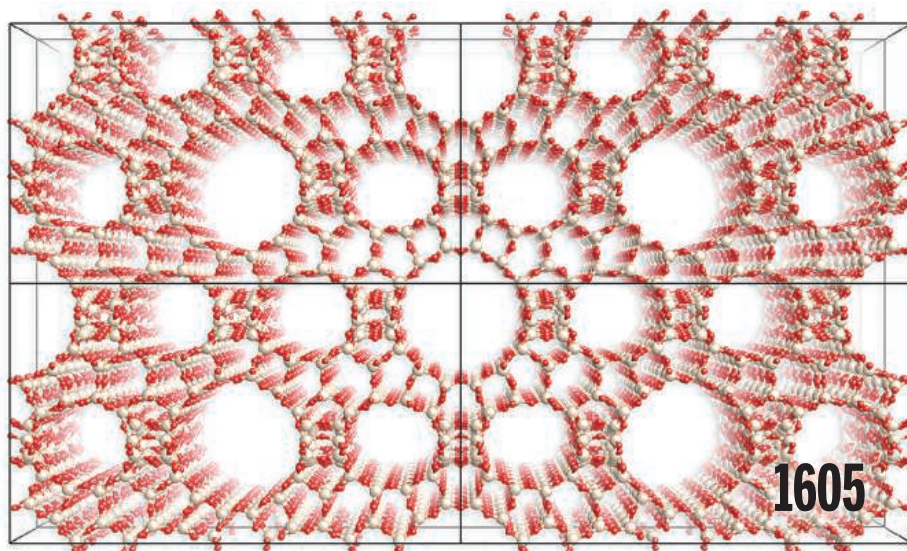
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its replication. The molecule can be delivered in pill form, which may lead to a COVID-19 treatment that can be used outside of a hospital setting. See page 1586. *Illustration: Jason Solo/The Jacky Winter Group*

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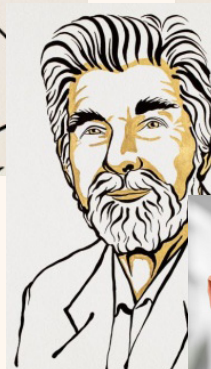
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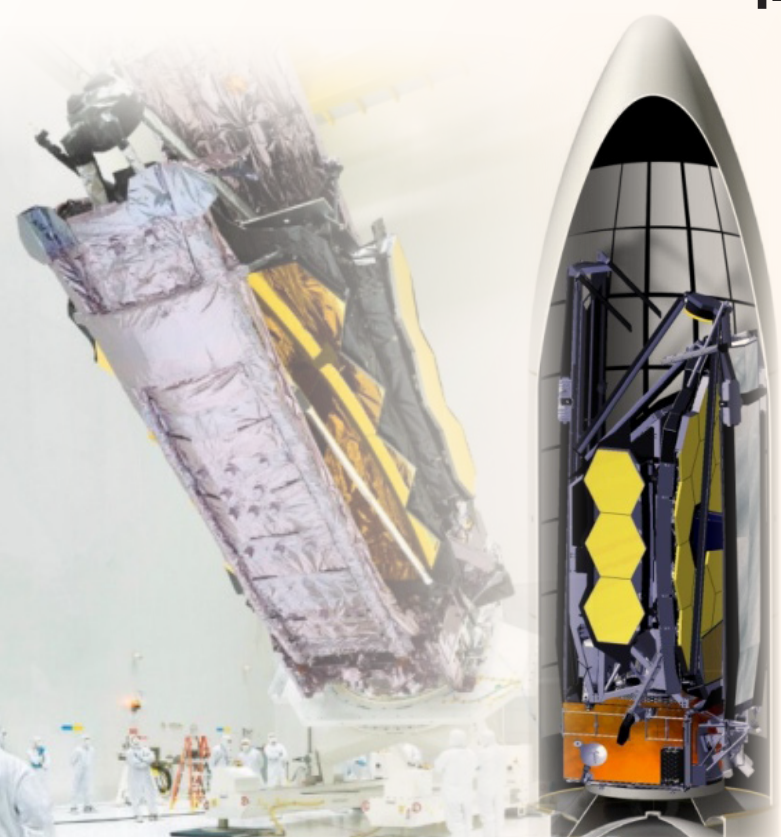
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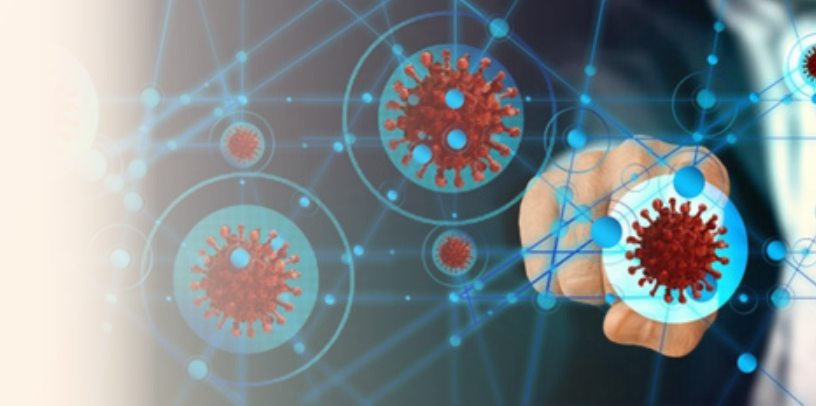
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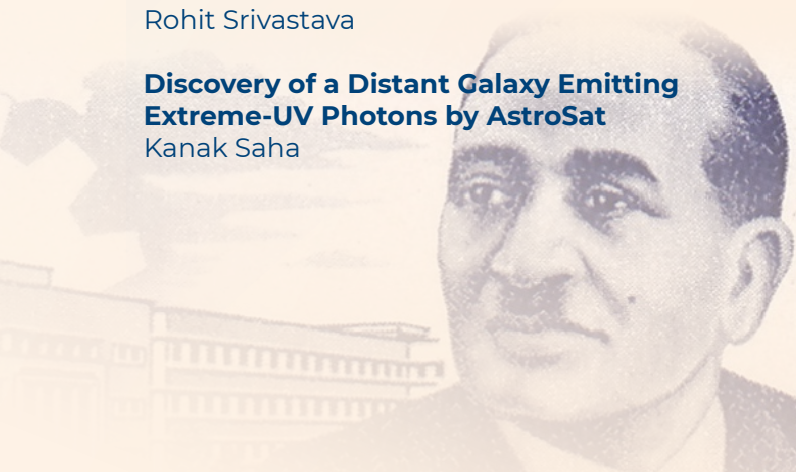
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[Reinstating universal health coverage on the global agenda](#)



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[A short cut to prevent postoperative atrial fibrillation](#)

[Cervical cancers avoided by HPV immunisation](#)

[Boosters appear effective, but are they always needed?](#)

[Global surveillance, research, and collaboration needed to improve understanding and management of long COVID](#)

[Offline: Is democracy good for your health?](#)



## WORLD REPORT

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[Hope for nutrition summit as global hunger spikes](#)

[Health warnings over UNRWA funding shortfall](#)

[Calls for international solutions to EU–Belarus border crisis](#)



## PERSPECTIVES

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[2021 Global Health Film Festival: platform for change](#)

[The many worlds of disability](#)

[Martin Griffiths: serving communities affected by violence](#)

[Knowing, seeing, and telling in medicine](#)



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[Obligations in a global health emergency](#)

[Obligations in a global health emergency – Authors' reply](#)

[Enabling physical activity for people living with disabilities](#)

[Enabling physical activity for people living with disabilities](#)

[Enabling physical activity for people living with disabilities](#)

[Enabling physical activity for people living with disabilities –  
Authors' reply](#)



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[Posterior left pericardiotomy for the prevention of atrial  
fibrillation after cardiac surgery: an adaptive, single-centre,  
single-blind, randomised, controlled trial](#)

[The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study](#)

[Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study](#)



## CLINICAL PICTURE

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[Fever, abdominal pain, serositis, arthralgia, hearing loss, proteinuria, and a family history: Muckle Wells syndrome](#)



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[Hypertrophic cardiomyopathy: a practical approach to guideline directed management](#)



## HEALTH POLICY

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[How an outbreak became a pandemic: a chronological analysis of crucial junctures and international obligations in the early months of the COVID-19 pandemic](#)

## EDITORIAL

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[Preventing violence against women: beyond 16 days](#)

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[Omicron SARS-CoV-2 variant: a new chapter in the COVID-19 pandemic](#)

[Tokyo Nutrition for Growth Summit 2021: an opportunity to accelerate the efforts towards achieving the SDGs](#)

[Angiography-derived quantitative flow ratio guidance of coronary intervention: measure twice, cut once](#)

[Long-acting amylin analogue for weight reduction](#)

[Inactivated SARS-CoV-2 vaccine \(BBV152\)-induced protection against symptomatic COVID-19](#)

[Offline: The origin story](#)

## WORLD REPORT

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[US Supreme Court expected to weaken abortion rights](#)

[What next for the Philippines' war on drugs?](#)

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[The healer as the enemy: attacking health care in war](#)

[Zarlasht Halaimzai: striving to provide a better future for refugees](#)

[Clay](#)

[Something in the water](#)

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[Prioritising immunisation across the life course](#)

[Prioritising immunisation across the life course – Authors' reply](#)

[High-dose budesonide for early COVID-19](#)

[High-dose budesonide for early COVID-19](#)

[High-dose budesonide for early COVID-19 – Authors' reply](#)

## DEPARTMENT OF ERROR

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## ARTICLES

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[Angiographic quantitative flow ratio-guided coronary intervention \(FAVOR III China\): a multicentre, randomised, sham-controlled trial](#)

[Once-weekly cagrilintide for weight management in people with overweight and obesity: a multicentre, randomised, double-blind, placebo-controlled and active-controlled, dose-finding phase 2 trial](#)

[Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine \(BBV152\): interim results of a randomised, double-blind, controlled, phase 3 trial](#)

## CLINICAL PICTURE

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[Oncogenic \*NTRK\* fusion in congenital spinal cord glioblastoma: sequencing directs treatment](#)

## HEALTH POLICY

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[Promoting COVID-19 vaccine acceptance: recommendations from the \*Lancet\* Commission on Vaccine Refusal, Acceptance, and Demand in the USA](#)

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[The evolution of the Italian National Health Service](#)

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[COVID-19: where do we go from here?](#)

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[PCI versus CABG for left main coronary artery disease: is the jury still out?](#)

[COV-BOOST: evidence to support rapid booster deployment](#)

[The political theatre of the UK's travel ban on South Africa](#)

[Global HIV efforts need to focus on key populations in LMICs](#)

[Universal health coverage must become a best buy for women](#)

[From a \*Lancet\* Commission to the NCDI Poverty Network: reaching the poorest billion through integration science](#)

[Winner of the 2021 Wakley Prize: something good enough](#)

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## ■ WORLD REPORT

[Russia–Ukraine tensions hampering health-care access](#)



[WHO and World Bank urge spending for UHC](#)

[2021: a year in review](#)

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[Another public health catastrophe](#)

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[The global oral health workforce](#)

[The global oral health workforce – Authors' reply](#)

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## ■ ARTICLES

[Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis](#)

[Safety and immunogenicity of seven COVID-19 vaccines as a third dose \(booster\) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK \(COV-BOOST\): a blinded, multicentre, randomised, controlled, phase 2 trial](#)

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[Safety and immunogenicity of concomitant administration of COVID-19 vaccines \(ChAdOx1 or BNT162b2\) with seasonal influenza vaccines in adults in the UK \(ComFluCOV\): a multicentre, randomised, controlled, phase 4 trial](#)

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 CLINICAL PICTURE

[Late presentation of hepatocellular carcinoma highlights the need for a public health programme to eliminate hepatitis B](#)

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[Head and neck cancer](#)

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[Revisiting academic health sciences systems a decade later: discovery to health to population to society](#)

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[Something good enough](#)



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December 2, 2021

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## NEW COVID-19

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Explore our collection of articles and resources on [Covid-19](#).

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### Comparative Effectiveness of BNT162b2 and mRNA-1273 Vaccines in U.S. Veterans

B.A. Dickerman and Others

DOI: 10.1056/NEJMoa2115463 | December 1, 2021

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### Covid-19 Vaccine Effectiveness in New York State

E.S. Rosenberg and Others

DOI: 10.1056/NEJMoa2116063 | December 1, 2021

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### Covid-19 mRNA Vaccines — Six of One, Half a Dozen of the Other

E.J. Rubin and D.L. Longo

DOI: 10.1056/NEJMe2117446 | December 1, 2021

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### Viral Dynamics of SARS-CoV-2 Variants in Vaccinated and Unvaccinated Persons

S.M. Kissler and Others

DOI: 10.1056/NEJMc2102507 | December 1, 2021

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## PERSPECTIVE

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### Fundamentals of Public Health: Using Policy Tools to Improve Population Health — Combating the U.S. Opioid Crisis

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C.L. Barry and B. Saloner

N Engl J Med 2021;385:2113-2116 | Published Online November 27, 2021

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## Decarbonizing the U.S. Health Sector — A Call to Action

V.J. Dzau, R. Levine, G. Barrett, and A. Witty

N Engl J Med 2021;385:2117-2119 | Published Online October 13, 2021

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## The Web We Weave

M. Hedlin

N Engl J Med 2021;385:2119-2121 | Published Online November 27, 2021

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## Is It Finally Time for a Medicare Dental Benefit?

L. Simon and W.V. Giannobile

N Engl J Med 2021;385:e80 | Published Online October 20, 2021

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### **ORIGINAL ARTICLES**

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## Randomized Trial of Cytoreductive Surgery for Relapsed Ovarian Cancer

P. Harter and Others

N Engl J Med 2021;385:2123-2131

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## Myocarditis after Covid-19 Vaccination in a Large Health Care Organization

G. Witberg and Others

N Engl J Med 2021;385:2132-2139 | Published Online October 6, 2021

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## Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel

D. Mevorach and Others

N Engl J Med 2021;385:2140-2149 | Published Online October 6, 2021

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## Edoxaban versus Vitamin K Antagonist for Atrial Fibrillation after TAVR

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N.M. Van Mieghem and Others

N Engl J Med 2021;385:2150-2160 | Published Online August 28, 2021

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## Milvexian for the Prevention of Venous Thromboembolism

J.I. Weitz and Others

N Engl J Med 2021;385:2161-2172 | Published Online November 15, 2021

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## REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19

D.M. Weinreich and Others

N Engl J Med 2021;385:e81 | Published Online September 29, 2021

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## 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer

K. Kalinsky and Others

DOI: 10.1056/NEJMoa2108873 | December 1, 2021

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### **REVIEW ARTICLE**

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## Spontaneous Intracranial Hypotension

W.I. Schievink

N Engl J Med 2021;385:2173-2178

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### **IMAGES IN CLINICAL MEDICINE**

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## Morel–Lavallée Lesion

Y.-H. Kim and H.-Y. Park

N Engl J Med 2021;385:2179 | Published Online November 27, 2021

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## Ectopic Tooth in the Nose

S. Khanna and M. Turner

N Engl J Med 2021;385:e82

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## CLINICAL PROBLEM-SOLVING

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### A “Fluid” Diagnosis

O. Albin and Others

N Engl J Med 2021;385:2180-2185

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## EDITORIALS

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### Recurrent Ovarian Cancer — Sculpting a Promising Future with Surgery

G.J. Gardner and D.S. Chi

N Engl J Med 2021;385:2187-2188

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### Receipt of mRNA Vaccine against Covid-19 and Myocarditis

A.L.P. Caforio

N Engl J Med 2021;385:2189-2190

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### Audio Interview: The Omicron Variant of SARS-CoV-2

E.J. Rubin, L.R. Baden, S.S. Abdool Karim, and S. Morrissey

N Engl J Med 2021;385:e96

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## CLINICAL IMPLICATIONS OF BASIC RESEARCH

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### Predicting Proteome-Scale Protein Structure with Artificial Intelligence

S.K. Burley, W. Arap, and R. Pasqualini

N Engl J Med 2021;385:2191-2194

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### BNT162b2 and ChAdOx1 nCoV-19 Vaccine Effectiveness against Death from the

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## Delta Variant

Published Online October 20, 2021

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## Toxic Effects from Ivermectin Use Associated with Prevention and Treatment of Covid-19

Published Online October 20, 2021

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## Benefits and Risks of Iron Interventions in Infants in Bangladesh

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## Mycophenolate Mofetil for Immune Thrombocytopenia

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## VITT after ChAdOx1 nCoV-19 Vaccination

Published Online November 3, 2021

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## Convalescent Plasma for Outpatients with Covid-19

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## Triple Therapy for Cystic Fibrosis *Phe508del*-Gating and -Residual Function Genotypes



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## NEW COVID-19

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Explore our collection of articles and resources on [Covid-19](#).

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### BNT162b2 Vaccine Booster and Mortality Due to Covid-19

R. Arbel and Others

DOI: 10.1056/NEJMoa2115624 | December 8, 2021

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### Protection against Covid-19 by BNT162b2 Booster across Age Groups

Y.M. Bar-On and Others

DOI: 10.1056/NEJMoa2115926 | December 8, 2021

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### Booster Doses and Prioritizing Lives Saved

M.K. Patel

DOI: 10.1056/NEJMe2117592 | December 8, 2021

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### Nursing Home Staff Vaccination and Covid-19 Outcomes

B.E. McGarry and Others

DOI: 10.1056/NEJMc2115674 | December 8, 2021

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### Tracking the Emergence of SARS-CoV-2 Alpha Variant in the United Kingdom

A.S. Walker and Others

DOI: 10.1056/NEJMc2103227 | December 8, 2021

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### Covid-19 and the Safety Net — Moving from Straining to Sustaining

J. Knudsen and D.A. Chokshi

N Engl J Med 2021;385:2209-2211 | Published Online December 4, 2021



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## Inequitable Access to Hospital Care — Protecting Disadvantaged Populations during Public Health Emergencies

D.B. White, L. Villarroel, and J.L. Hick

N Engl J Med 2021;385:2211-2214 | Published Online December 4, 2021

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## Runner-up in the 2021 NEJM Medical Fiction Contest: Emperor of the Empire

M.S. Bravo

N Engl J Med 2021;385:2215-2217 | Published Online October 13, 2021

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### **ORIGINAL ARTICLES**

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## Phase 3 Trials of Tapinarof Cream for Plaque Psoriasis

M.G. Lebwohl and Others

N Engl J Med 2021;385:2219-2229

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## Dupilumab in Children with Uncontrolled Moderate-to-Severe Asthma

L.B. Bacharier and Others

N Engl J Med 2021;385:2230-2240

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## Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents

K. Ali and Others

N Engl J Med 2021;385:2241-2251 | Published Online August 11, 2021

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## Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes

B. Pitt and Others

N Engl J Med 2021;385:2252-2263 | Published Online August 28, 2021

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## Brief Report: Transgenic Epidermal Cultures for Junctional Epidermolysis Bullosa — 5-Year Outcomes

M. Kueckelhaus and Others

N Engl J Med 2021;385:2264-2270

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## Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar

H. Chemaitelly and Others

N Engl J Med 2021;385:e83 | Published Online October 6, 2021

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## Waning Immune Humoral Response to BNT162b2 Covid-19 Vaccine over 6 Months

E.G. Levin and Others

N Engl J Med 2021;385:e84 | Published Online October 6, 2021

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## Waning Immunity after the BNT162b2 Vaccine in Israel

Y. Goldberg and Others

N Engl J Med 2021;385:e85 | Published Online October 27, 2021

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### **SPECIAL ARTICLE**

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## Abortion Safety and Use with Normally Prescribed Mifepristone in Canada

L. Schummers and Others

DOI: 10.1056/NEJMsa2109779 | December 8, 2021

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### **CLINICAL PRACTICE**

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## Latent Tuberculosis Infection

M. Shah and S.E. Dorman

N Engl J Med 2021;385:2271-2280

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### **IMAGES IN CLINICAL MEDICINE**

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## Transverse Nasal Creases

B. Zhang and L. Ma

N Engl J Med 2021;385:2281 | Published Online December 4, 2021

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## Congenital Langerhans-Cell Histiocytosis

A. Kallesh and V.S. Kumar

N Engl J Med 2021;385:e86

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### CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

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## Case 37-2021: A 60-Year-Old Man with Fevers, Fatigue, Arthralgias, a Mouth Ulcer, and a Rash

Z.S. Wallace and Others

N Engl J Med 2021;385:2282-2293

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### EDITORIALS

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## AhR Modulating Agent for the Topical Therapy of Plaque Psoriasis

T. Bieber

N Engl J Med 2021;385:2295-2296

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## Need for Racial and Ethnic Diversity in Asthma Precision Medicine

E. González Burchard and L.N. Borrell

N Engl J Med 2021;385:2297-2298

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## Audio Interview: Waning Immunity against SARS-CoV-2

E.J. Rubin, L.R. Baden, and S. Morrissey

N Engl J Med 2021;385:e99

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## Adverse Effects after BNT162b2 Vaccine and SARS-CoV-2 Infection, According to Age and Sex

Published Online October 27, 2021

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## Effectiveness of the mRNA-1273 Vaccine during a SARS-CoV-2 Delta Outbreak in a Prison

Published Online October 20, 2021



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## NEW COVID-19

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### Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico

L.M. Dunkle and Others

DOI: 10.1056/NEJMoa2116185 | December 15, 2021

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### Efficacy of Natural Immunity against SARS-CoV-2 Reinfection with the Beta Variant

H. Chemaitelly, R. Bertollini, and L.J. Abu-Raddad

DOI: 10.1056/NEJMc2110300 | December 15, 2021

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### Universal Coronavirus Vaccines — An Urgent Need

D.M. Morens, J.K. Taubenberger, and A.S. Fauci

DOI: 10.1056/NEJMp2118468 | December 15, 2021

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### The Wild West of Checkpoint Inhibitor Development

J.A. Beaver and R. Pazdur

DOI: 10.1056/NEJMp2116863 | December 15, 2021

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### A Failure to Disseminate Transformative Science — HIV Treatment as Prevention, 10 Years On

J. Bor, D. Onoya, B. Richman, and K.H. Mayer

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N Engl J Med 2021;385:2305-2307 | Published Online December 11, 2021

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### E66.01 and Our Culture of Shame

S. Hagan

N Engl J Med 2021;385:2307-2309 | Published Online December 11, 2021

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### Ms. Omega One

M. Wilbur

N Engl J Med 2021;385:2309-2311 | Published Online December 11, 2021

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### Daprodustat for the Treatment of Anemia in Patients Not Undergoing Dialysis

A.K. Singh and Others

N Engl J Med 2021;385:2313-2324 | Published Online November 5, 2021

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### Daprodustat for the Treatment of Anemia in Patients Undergoing Dialysis

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N Engl J Med 2021;385:2325-2335 | Published Online November 5, 2021

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### 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer

K. Kalinsky and Others

N Engl J Med 2021;385:2336-2347 | Published Online December 1, 2021

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### Phase 3 Safety and Efficacy of AZD1222 (ChAdOx1 nCoV-19) Covid-19 Vaccine

A.R. Falsey and Others

N Engl J Med 2021;385:2348-2360 | Published Online September 29, 2021

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### Effectiveness of mRNA Covid-19 Vaccine among U.S. Health Care Personnel

T. Pilishvili and Others

## Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma

M.R. Bishop and Others

DOI: 10.1056/NEJMoa2116596 | December 14, 2021

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## Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma

H. Tilly and Others

DOI: 10.1056/NEJMoa2115304 | December 14, 2021

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## Biologic and Clinical Efficacy of LentiGlobin for Sickle Cell Disease

J. Kanter and Others

DOI: 10.1056/NEJMoa2117175 | December 12, 2021

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## Brief Report: Acute Myeloid Leukemia Case after Gene Therapy for Sickle Cell Disease

S. Goyal and Others

DOI: 10.1056/NEJMoa2109167 | December 12, 2021

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## Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma

F.L. Locke and Others

DOI: 10.1056/NEJMoa2116133 | December 11, 2021

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## Betibeglogene Autotemcel Gene Therapy for Non- $\beta^0/\beta^0$ Genotype $\beta$ -Thalassemia

F. Locatelli and Others

DOI: 10.1056/NEJMoa2113206 | December 11, 2021

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## Pulmonary Arterial Hypertension

P.M. Hassoun

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N Engl J Med 2021;385:2361-2376

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**IMAGES IN CLINICAL MEDICINE**

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**Tongue Necrosis in Giant-Cell Arteritis**

B. Dilly and C. Bomahou

N Engl J Med 2021;385:2377

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**Linear Darier's Disease**

T.D. McKinley and M. Maroon

N Engl J Med 2021;385:e91 | Published Online December 11, 2021

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**CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL**

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**Case 38-2021: A 76-Year-Old Woman with Abdominal Pain, Weight Loss, and Memory Impairment**

L.L. Willett and Others

N Engl J Med 2021;385:2378-2388

**CME**

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**Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors for Anemia in CKD**

P. Parfrey

N Engl J Med 2021;385:2390-2391 | Published Online November 5, 2021

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**CAR T-Cell Therapy for Large B-Cell Lymphoma — Who, When, and How?**

M. Roschewski, D.L. Longo, and W.H. Wilson

DOI: 10.1056/NEJMe2118899 | December 14, 2021

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## Audio Interview: How Much Protection Does Prior SARS-CoV-2 Infection Provide?

E.J. Rubin, L.R. Baden, and S. Morrissey  
N Engl J Med 2021;385:e100

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### CLINICAL IMPLICATIONS OF BASIC RESEARCH

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## A Nobel Prize for Sensational Research

M.J. Zylka  
N Engl J Med 2021;385:2392-2394 | Published Online November 24, 2021

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### CORRESPONDENCE

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## Antibiotics versus Appendectomy for Acute Appendicitis — Longer-Term Outcomes

Published Online October 25, 2021

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## Neutralization of the SARS-CoV-2 Mu Variant by Convalescent and Vaccine Serum

Published Online November 3, 2021

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## Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant

Published Online November 10, 2021

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## SARS-CoV-2 Infection in Vaccinated Health Care Workers

DOI: 10.1056/NEJMc2117119 | December 15, 2021





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## NEW COVID-19

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### Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients

R.L. Gottlieb and Others

DOI: 10.1056/NEJMoa2116846 | December 22, 2021

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### The Goldilocks Time for Remdesivir — Is Any Indication Just Right?

E.L. Heil and S. Kottlilil

DOI: 10.1056/NEJMe2118579 | December 22, 2021

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### Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients

A. Jayk Bernal and Others

DOI: 10.1056/NEJMoa2116044 | December 16, 2021

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### Molnupiravir — A Step toward Orally Bioavailable Therapies for Covid-19

R. Whitley

DOI: 10.1056/NEJMe2117814 | December 16, 2021

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### VITT and Second Doses of Covid-19 Vaccine

J. Lacy, S. Pavord, and K.E. Brown

DOI: 10.1056/NEJMc2118507 | December 22, 2021

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### Effects of BNT162b2 Covid-19 Vaccine Booster in Long-Term Care Facilities in Israel

K. Muhsen and Others

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DOI: 10.1056/NEJMc2117385 | December 22, 2021

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“Please Don’t Keep Me”

A. Drutchas

DOI: 10.1056/NEJMp2115096 | December 22, 2021

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In Clinical Care, What Will Amazon Deliver?

E. Rourke

N Engl J Med 2021;385:2401-2403 | Published Online December 18, 2021

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Covid-19 Vaccination in American Indians and Alaska Natives — Lessons from Effective Community Responses

R. Foxworth and Others

N Engl J Med 2021;385:2403-2406 | Published Online December 18, 2021

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Tobacco-free Nicotine — New Name, Same Scheme?

S.N. Cwalina, R. McConnell, N.L. Benowitz, and J.L. Barrington-Trimis

N Engl J Med 2021;385:2406-2408 | Published Online December 18, 2021

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A Divisive Ruling on Devices — *Genus Medical Technologies v. FDA*

P.J. Zettler, E.Y. Adashi, and I.G. Cohen

N Engl J Med 2021;385:2409-2411 | Published Online November 24, 2021

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Relief in Sight — Estimated Savings under Medicare Part D Redesign

S.B. Dusetzina

N Engl J Med 2021;385:e93 | Published Online November 10, 2021

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**BNT162b2 Vaccine Booster and Mortality Due to Covid-19**

R. Arbel and Others

N Engl J Med 2021;385:2413-2420 | Published Online December 8, 2021

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**Protection against Covid-19 by BNT162b2 Booster across Age Groups**

Y.M. Bar-On and Others

N Engl J Med 2021;385:2421-2430 | Published Online December 8, 2021

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**Trial of Spesolimab for Generalized Pustular Psoriasis**

H. Bachelez and Others

N Engl J Med 2021;385:2431-2440

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**Multicomponent Strategy with Decentralized Molecular Testing for Tuberculosis**

A. Cattamanchi and Others

N Engl J Med 2021;385:2441-2450

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**Frontiers in Medicine: Immune and Genome Engineering as the Future of Transplantable Tissue**

J. Elisseeff, S.F. Badylak, and J.D. Boeke

N Engl J Med 2021;385:2451-2462

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**IMAGES IN CLINICAL MEDICINE**

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**Minocycline-Induced Hyperpigmentation**

S. Katayama and M. Ota

N Engl J Med 2021;385:2463 | Published Online December 18, 2021

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## Pupillary Light–Near Dissociation

E. La Corte and M. Martinoni  
N Engl J Med 2021;385:e94

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### CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

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## Case 39-2021: A 26-Year-Old Woman with Respiratory Failure and Altered Mental Status

A. Kadar and Others  
N Engl J Med 2021;385:2464-2474

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### EDITORIALS

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## Booster Doses and Prioritizing Lives Saved

M.K. Patel  
N Engl J Med 2021;385:2476-2477 | Published Online December 8, 2021

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## Audio Interview: A Potential New Agent to Treat Covid-19

E.J. Rubin, L.R. Baden, and S. Morrissey  
N Engl J Med 2021;385:e101

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### MEDICINE AND SOCIETY

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## Consultative Medicine — An Emerging Specialty for Patients with Perplexing Conditions

L.N. Geng, A. Verghese, and J.C. Tilburt  
N Engl J Med 2021;385:2478-2484

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[Phase 3 Trial of mRNA-1273 during the Delta-Variant Surge](#)

Published Online November 3, 2021

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[Severity of SARS-CoV-2 Reinfections as Compared with Primary Infections](#)

Published Online November 24, 2021

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[Viral Dynamics of SARS-CoV-2 Variants in Vaccinated and Unvaccinated Persons](#)

Published Online December 1, 2021

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[Salt Substitute and Cardiovascular Events and Death](#)

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[Lutetium-177–PSMA-617 for Prostate Cancer](#)

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[Clinical Features of VITT](#)

DOI: 10.1056/NEJMc2118473 | December 22, 2021



December 30, 2021

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**NEW COVID-19**

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Explore our collection of articles and resources on [Covid-19](#).

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Effectiveness of BNT162b2 Vaccine against Omicron Variant in South Africa

S. Collie and Others

DOI: 10.1056/NEJMc2119270 | December 29, 2021

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Third BNT162b2 Vaccination Neutralization of SARS-CoV-2 Omicron Infection

I. Nemet and Others

DOI: 10.1056/NEJMc2119358 | December 29, 2021

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Adolescents, Parents, and Covid-19 Vaccination — Who Should Decide?

S. McGrew and H.A. Taylor

DOI: 10.1056/NEJMp2116771 | December 29, 2021

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First Impressions — Should We Include Race or Ethnicity at the Beginning of Clinical Case Presentations?

A.S. Brett and C.W. Goodman

N Engl J Med 2021;385:2497-2499 | Published Online December 25, 2021

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Calling Out Aversive Racism in Academic Medicine

C.L. Chen, G.J. Gold, M. Cannesson, and J.M. Lucero

N Engl J Med 2021;385:2499-2501 | Published Online December 25, 2021

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## Closing the Gender Pay Gap in Medicine

A.S. Gottlieb and R. Jaggi

N Engl J Med 2021;385:2501-2504 | Published Online October 20, 2021

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## Trust, Faith, and Covid

E. Rittenberg

N Engl J Med 2021;385:2504-2505 | Published Online December 25, 2021

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### ORIGINAL ARTICLES

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## Chlorthalidone for Hypertension in Advanced Chronic Kidney Disease

R. Agarwal and Others

N Engl J Med 2021;385:2507-2519 | Published Online November 5, 2021

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## Ticagrelor versus Clopidogrel in *CYP2C19* Loss-of-Function Carriers with Stroke or TIA

Y. Wang and Others

N Engl J Med 2021;385:2520-2530 | Published Online October 28, 2021

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## Dolutegravir as First- or Second-Line Treatment for HIV-1 Infection in Children

A. Turkova and Others

N Engl J Med 2021;385:2531-2543

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## Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation

S. Desch and Others

N Engl J Med 2021;385:2544-2553 | Published Online August 29, 2021

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### CLINICAL PRACTICE

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## Determination of Brain Death

D.M. Greer

N Engl J Med 2021;385:2554-2561

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### IMAGES IN CLINICAL MEDICINE

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## Carcinoma en Cuirasse

V. Sharma and A. Kumar

N Engl J Med 2021;385:2562

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## Untreated Chronic Gout

T. Chen and D.-L. Ma

N Engl J Med 2021;385:e97 | Published Online December 25, 2021

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### CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

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## Case 40-2021: A 9-Year-Old Boy with Transient Weakness, Facial Droop, and Slurred Speech

M.E. Bernson-Leung, O. Rapalino, M.A. Walker, and W.E. Butler

N Engl J Med 2021;385:2563-2572

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## Chlorthalidone in Advanced Chronic Kidney Disease — Have We Missed a Trick?

D.C. Wheeler

N Engl J Med 2021;385:2574-2575

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## Genetic Profile–Guided Therapy for Stroke?

S.K. Feske



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N Engl J Med 2021;385:2576-2577

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## Employees of the Massachusetts Medical Society in 2021

E.J. Rubin

N Engl J Med 2021;385:2578

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## Audio Interview: Covid-19 Vaccination and the Omicron Variant

E.J. Rubin, L.R. Baden, and S. Morrissey

N Engl J Med 2021;385:e102

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### CLINICAL IMPLICATIONS OF BASIC RESEARCH

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## A Noble Quest for Simplicity in the Chiral World

S.B. Tsogoeva

N Engl J Med 2021;385:2579-2581 | Published Online November 24, 2021

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## Tracking the Emergence of SARS-CoV-2 Alpha Variant in the United Kingdom

Published Online December 8, 2021

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## Efficacy of Natural Immunity against SARS-CoV-2 Reinfection with the Beta Variant

Published Online December 15, 2021

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## Maintenance or Discontinuation of Antidepressants in Primary Care

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## Trial of Intensive Blood-Pressure Control in Older Patients with Hypertension

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## Placement of a Double-Lumen Endotracheal Tube

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**Race and Health — A Persistent American Dilemma**

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N Engl J Med 2021;385:e98

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