



Cover image: Pictured is a *Pocillopora* coral showing the golden-brown cells of *Symbiodinium*, an endosymbiotic dinoflagellate, inside its tissues. Madeleine J. H. van Oppen et al. reviewed studies that reveal the risks and benefits of artificially manipulating the evolution of organisms to prepare them for imminent climate change. The authors advocate attempts to help *Symbiodinium* species adapt to elevated temperatures and other altered environmental conditions to increase stress tolerance in corals inoculated with the endosymbionts. See the article by van Oppen et al. on pages 2307–2313. Image courtesy of Gergely Torda (James Cook University, College of Marine and Environmental Sciences, Townsville, Australia).

From the Cover

- 2307 Assisting coral reef resilience
- E911 Root niches and their microbiomes
- 2485 Coordinated gene copy number variation
- 2539 Perceived nicotine content of cigarettes
- 2617 Organismal metabolism and carbon flow in the environment

Contents

THIS WEEK IN PNAS

- 2293 **In This Issue**

LETTERS (ONLINE ONLY)

- E820 **Role of dairy in the carbon footprint of US beef**
Nicole Tichenor
- E822 **Reply to Tichenor: Proposed update to beef greenhouse gas footprint is numerically questionable and well within current uncertainty bounds**
Gidon Eshel, Alon Shepon, Tamar Makov, and Ron Milo
- E824 **Perpetual muscle PDH activation in PDH kinase knockout mice protects against high-fat feeding–induced muscle insulin resistance**
Dumitru Constantin-Teodosiu, Francis B. Stephens, and Paul L. Greenhaff
- E825 **Reply to Constantin-Teodosiu et al.: Mice with genetic PDH activation are not protected from high-fat diet–induced muscle insulin resistance**
Max C. Petersen, Yasmeen Rahimi, Joao-Paulo G. Camporez, Dominik Pesta, Rachel J. Perry, Michael J. Jurczak, Gary W. Cline, and Gerald I. Shulman



Free online through the PNAS open access option.

SCIENCE AND CULTURE—*How science intersects with culture*

- 2295 **Science and Culture: Data visualization nurtures an artistic movement**
J. D. Talasek

INNER WORKINGS—*An over-the-shoulder look at scientists at work*

- 2296 **Inner Workings: Endoliths hunker down and survive in extreme environments**
Amber Dance

COMMENTARIES

- 2297 **Heavy-chain receptor editing unbound**
Garnett Kelsoe
→ See companion articles on pages E450 and E458 in issue 5 of volume 112
- 2299 **Root surface as a frontier for plant microbiome research**
Marcel G. A. van der Heijden and Klaus Schlaeppi
→ See companion article on page E911
- 2301 **Beliefs modulate the effects of drugs on the human brain**
Nora D. Volkow and Ruben Baler
→ See companion article on page 2539
- 2303 **Individuals scale up carbon flow in ecosystems**
Just Cebrian
→ See companion article on page 2617


PNAS PLUS

2305 Significance Statements

→ *Brief statements written by the authors about the significance of their papers.*

PERSPECTIVE


2307 Building coral reef resilience through assisted evolution

 Madeleine J. H. van Oppen, James K. Oliver, Hollie M. Putnam, and Ruth D. Gates

PHYSICAL SCIENCES

APPLIED PHYSICAL SCIENCES


2314 Simultaneous cryo X-ray ptychographic and fluorescence microscopy of green algae

 Junjing Deng, David J. Vine, Si Chen, Youssef S. G. Nashed, Qiaoling Jin, Nicholas W. Phillips, Tom Peterka, Rob Ross, Stefan Vogt, and Chris J. Jacobsen

2320 Lack of exercise leads to significant and reversible loss of scale invariance in both aged and young mice

Changgui Gu, Claudia P. Coomans, Kun Hu, Frank A. J. L. Scheer, H. Eugene Stanley, and Johanna H. Meijer

2325 Toward link predictability of complex networks


 Linyuan Lü, Liming Pan, Tao Zhou, Yi-Cheng Zhang, and H. Eugene Stanley

2331 Probing equilibrium glass flow up to exapoise viscosities

Eva Arianna Aurelia Pogna, Cristian Rodríguez-Tinoco, Giulio Cerullo, Carino Ferrante, Javier Rodríguez-Viejo, and Tullio Scopigno

CHEMISTRY

2337 Efficient solar-to-fuels production from a hybrid microbial–water-splitting catalyst system

 Joseph P. Torella, Christopher J. Gagliardi, Janice S. Chen, D. Kwabena Bediako, Brendan Colón, Jeffery C. Way, Pamela A. Silver, and Daniel G. Nocera

2343 Highly efficient conversion of superoxide to oxygen using hydrophilic carbon clusters

Errol L. G. Samuel, Daniela C. Marcano, Vladimir Berka, Brittany R. Bitner, Gang Wu, Austin Potter, Roderic H. Fabian, Robia G. Pautler, Thomas A. Kent, Ah-Lim Tsai, and James M. Tour

2437 Mechanism of initiation of aggregation of p53 revealed by Φ -value analysis

GuoZhen Wang and Alan R. Fersht

2443 Propagation of aggregated p53: Cross-reaction and coaggregation vs. seeding

GuoZhen Wang and Alan R. Fersht

EARTH, ATMOSPHERIC, AND PLANETARY SCIENCES

2349 Widespread pollution of the South American atmosphere predates the industrial revolution by 240 y

Chiara Uglietti, Paolo Gabrielli, Colin A. Cooke, Paul Vallelonga, and Lonnie G. Thompson

2355 Erosion during extreme flood events dominates Holocene canyon evolution in northeast Iceland



Edwin R. C. Baynes, Mikaël Attal, Samuel Niedermann, Linda A. Kirstein, Andrew J. Dugmore, and Mark Naylor

ENGINEERING

E826 Visualizing monolayers with a water-soluble fluorophore to quantify adsorption, desorption, and the double layer

Ian C. Shieh and Joseph A. Zasadzinski

PHYSICS

2361 Calorimetric glass transition in a mean-field theory approach

Manuel Sebastian Mariani, Giorgio Parisi, and Corrado Rainone

2367 Classification of charge density waves based on their nature



Xuetao Zhu, Yanwei Cao, Jiandi Zhang, E. W. Plummer, and Jiandong Guo

2372 Penta-graphene: A new carbon allotrope

Shunhong Zhang, Jian Zhou, Qian Wang, Xiaoshuang Chen, Yoshiyuki Kawazoe, and Puru Jena

2378 Warning signals for eruptive events in spreading fires

Jerome M. Fox and George M. Whitesides

2384 Correlation between ground state and orbital anisotropy in heavy fermion materials



Thomas Willers, Fabio Strigari, Zhiwei Hu, Violetta Sessi, Nicholas B. Brookes, Eric D. Bauer, John L. Sarrao, J. D. Thompson, Arata Tanaka, Steffen Wirth, Liu Hao Tjeng, and Andrea Severing

2533 Critical and maximally informative encoding between neural populations in the retina



David B. Kastner, Stephen A. Baccus, and Tatyana O. Sharpee

2611 Greedy scheduling of cellular self-replication leads to optimal doubling times with a log-Frechet distribution



Rami Pugatch

STATISTICS

2479 Massively expedited genome-wide heritability analysis (MEGHA)



Tian Ge, Thomas E. Nichols, Phil H. Lee, Avram J. Holmes, Joshua L. Roffman, Randy L. Buckner, Mert R. Sabuncu, and Jordan W. Smoller


SOCIAL SCIENCES

PSYCHOLOGICAL AND COGNITIVE SCIENCES

2389 Human language reveals a universal positivity bias



Peter Sheridan Dodds, Eric M. Clark, Suma Desu, Morgan R. Frank, Andrew J. Reagan, Jake Ryland Williams, Lewis Mitchell, Kameron Decker Harris, Isabel M. Kloumann, James P. Bagrow, Karine Megerdooian, Matthew T. McMahon, Brian F. Tivnan, and Christopher M. Danforth

- 2539  **Belief about nicotine selectively modulates value and reward prediction error signals in smokers**
Xiaosi Gu, Terry Lohrenz, Ramiro Salas, Philip R. Baldwin, Alireza Soltani, Ulrich Kirk, Paul M. Cinciripini, and P. Read Montague
→ See Commentary on page 2301

SOCIAL SCIENCES


- 2395  **Validating vignette and conjoint survey experiments against real-world behavior**
Jens Hainmueller, Dominik Hangartner, and Teppei Yamamoto

BIOLOGICAL SCIENCES



APPLIED BIOLOGICAL SCIENCES

- 2401 **Glucose-responsive insulin activity by covalent modification with aliphatic phenylboronic acid conjugates**
Danny Hung-Chieh Chou, Matthew J. Webber, Benjamin C. Tang, Amy B. Lin, Lavanya S. Thapa, David Deng, Jonathan V. Truong, Abel B. Cortinas, Robert Langer, and Daniel G. Anderson


BIOCHEMISTRY

- E836 **C-terminal sequence of amyloid-resistant type F apolipoprotein A-II inhibits amyloid fibril formation of apolipoprotein A-II in mice**
Jinko Sawashita, Beiru Zhang, Kazuhiro Hasegawa, Masayuki Mori, Hironobu Naiki, Fuyuki Kametani, and Keiichi Higuchi (樋口京一)
- 2407 **Thermodynamic mechanism for inhibition of lactose permease by the phosphotransferase protein IIA^{Glc}**
Parameswaran Hariharan, Dhandayuthapani Balasubramaniam, Alan Peterkofsky, H. Ronald Kaback, and Lan Guan
- 2413 **Structures of the G β -CCT and PhLP1-G β -CCT complexes reveal a mechanism for G-protein β -subunit folding and G $\beta\gamma$ dimer assembly**
Rebecca L. Plimpton, Jorge Cuéllar, Chun Wan J. Lai, Takuma Aoba, Aman Makaju, Sarah Franklin, Andrew D. Mathis, John T. Prince, José L. Carrascosa, José M. Valpuesta, and Barry M. Willardson
- 2419 **Visualization of a radical B₁₂ enzyme with its G-protein chaperone**
Marco Jost, Valentin Cracan, Paul A. Hubbard, Ruma Banerjee, and Catherine L. Drennan
- 2425 **In-cell SHAPE reveals that free 30S ribosome subunits are in the inactive state**
Jennifer L. McGinnis, Qi Liu, Christopher A. Lavender, Aishwarya Devaraj, Sean P. McClory, Kurt Fredrick, and Kevin M. Weeks
- 2431  **Tetrahydrobiopterin and alkylglycerol monooxygenase substantially alter the murine macrophage lipidome**
Katrin Watschinger, Markus A. Keller, Eileen McNeill, Mohammad T. Alam, Steven Lai, Sabrina Sailer, Veronika Rauch, Jyoti Patel, Albin Hermetter, Georg Golderer, Stephan Geley, Gabriele Werner-Felmayer, Robert S. Plumb, Giuseppe Astarita, Markus Ralser, Keith M. Channon, and Ernst R. Werner

BIOPHYSICS AND COMPUTATIONAL BIOLOGY

- E826 **Visualizing monolayers with a water-soluble fluorophore to quantify adsorption, desorption, and the double layer**
Ian C. Shieh and Joseph A. Zasadzinski
- 2314  **Simultaneous cryo X-ray ptychographic and fluorescence microscopy of green algae**
Junjing Deng, David J. Vine, Si Chen, Youssef S. G. Nashed, Qiaoling Jin, Nicholas W. Phillips, Tom Peterka, Rob Ross, Stefan Vogt, and Chris J. Jacobsen
- 2437 **Mechanism of initiation of aggregation of p53 revealed by Φ -value analysis**
GuoZhen Wang and Alan R. Fersht
- 2443 **Propagation of aggregated p53: Cross-reaction and coaggregation vs. seeding**
GuoZhen Wang and Alan R. Fersht
- 2449  **Lemon-shaped halo archaeal virus His1 with uniform tail but variable capsid structure**
Chuan Hong, Maija K. Pietilä, Caroline J. Fu, Michael F. Schmid, Dennis H. Bamford, and Wah Chiu
- 2455 **Bacterial chemoreceptor dynamics correlate with activity state and are coupled over long distances**
Dipanjan Samanta, Peter P. Borbat, Boris Dzikovski, Jack H. Freed, and Brian R. Crane
- 2461 **Localizing a gate in CFTR**
Xiaolong Gao and Tzyh-Chang Hwang



CELL BIOLOGY

- 2467  **Silencing LRH-1 in colon cancer cell lines impairs proliferation and alters gene expression programs**
James R. Bayrer, Sridevi Mulkamala, Elena P. Sablin, Paul Webb, and Robert J. Fletterick
- 2473 **Cholesterol uptake disruption, in association with chemotherapy, is a promising combined metabolic therapy for pancreatic adenocarcinoma**
Fabienne Guillaumond, Ghislain Bidaut, Mehdi Ouaisi, Stéphane Servais, Victoire Gourirand, Orianne Olivares, Sophie Lac, Laurence Borge, Julie Roques, Odile Gayet, Michelle Pinault, Cyrille Guimaraes, Jérémy Nigri, Céline Loncle, Marie-Noëlle Lavaut, Stéphane Garcia, Anne Tailleux, Bart Staels, Ezequiel Calvo, Richard Tomasini, Juan Lucio Iovanna, and Sophie Vasseur

EVOLUTION

- E846 **Convergence of ion channel genome content in early animal evolution**
Benjamin J. Liebeskind, David M. Hillis, and Harold H. Zakon

GENETICS

- E852  **Constraints on the evolution of a *doublesex* target gene arising from *doublesex*'s pleiotropic deployment**
Shengzhan D. Luo and Bruce S. Baker
- 2479  **Massively expedited genome-wide heritability analysis (MEGHA)**
Tian Ge, Thomas E. Nichols, Phil H. Lee, Avram J. Holmes, Joshua L. Roffman, Randy L. Buckner, Mert R. Sabuncu, and Jordan W. Smoller

2485 **Concerted copy number variation balances ribosomal DNA dosage in human and mouse genomes**
John G. Gibbons, Alan T. Branco, Susana A. Godinho, Shoukai Yu, and Bernardo Lemos

2491 **Extensive tissue-related and allele-related mtDNA heteroplasmy suggests positive selection for somatic mutations**
Mingkun Li, Roland Schröder, Shengyu Ni, Burkhard Madea, and Mark Stoneking

IMMUNOLOGY AND INFLAMMATION

E862 **Automated analysis of high-throughput B-cell sequencing data reveals a high frequency of novel immunoglobulin V gene segment alleles**
Daniel Gadala-Maria, Gur Yaari, Mohamed Uduman, and Steven H. Kleinstein

2497 **Extracellular forms of IL-37 inhibit innate inflammation in vitro and in vivo but require the IL-1 family decoy receptor IL-1R8**
Suzhao Li, C. Preston Neff, Kristina Barber, Jaewoo Hong, Yuchun Luo, Tania Azam, Brent E. Palmer, Mayumi Fujita, Cecilia Garlanda, Alberto Mantovani, Soohyun Kim, and Charles Anthony Dinarello

MEDICAL SCIENCES

2503 **Glucagon receptor antibody completely suppresses type 1 diabetes phenotype without insulin by disrupting a novel diabetogenic pathway**
May-Yun Wang, Hai Yan, Zhiqing Shi, Matthew R. Evans, Xinxin Yu, Young Lee, Shihuei Chen, Annie Williams, Jacques Philippe, Michael G. Roth, and Roger H. Unger

2509 **Low expression of CD39 on regulatory T cells as a biomarker for resistance to methotrexate therapy in rheumatoid arthritis**
Raphael Sanches Peres, Foo Y. Liew, Jhimmy Talbot, Vanessa Carregaro, Rene D. Oliveira, Sergio L. Almeida, Rafael F. O. França, Paula B. Donate, Larissa G. Pinto, Flavia I. S. Ferreira, Diego L. Costa, Daniel P. Demarque, Dayana Rubio Gouvea, Norberto P. Lopes, Regina Helena C. Queiroz, Joao Santana Silva, Florencio Figueiredo, Jose Carlos Alves-Filho, Thiago M. Cunha, Sérgio H. Ferreira, Paulo Louzada-Junior, and Fernando Q. Cunha

2515 **Discovery and horizontal follow-up of an autoantibody signature in human prostate cancer**
Paul J. Mintz, Anna Cecilia Rietz, Marina Cardó-Vila, Michael G. Ozawa, Eleonora Dondossola, Kim-Anh Do, Jeri Kim, Patricia Troncoso, Christopher J. Logothetis, Richard L. Sidman, Renata Pasqualini, and Wadih Arap

2521 **Ligand-directed targeting of lymphatic vessels uncovers mechanistic insights in melanoma metastasis**
Dawn R. Christianson, Andrey S. Dobroff, Bettina Proneth, Amado J. Zurita, Ahmad Salameh, Eleonora Dondossola, Jun Makino, Cristian G. Bologa, Tracey L. Smith, Virginia J. Yao, Tiffany L. Calderone, David J. O'Connell, Tudor I. Oprea, Kazunori Kataoka, Dolores J. Cahill, Jeffrey E. Gershenwald, Richard L. Sidman, Wadih Arap, and Renata Pasqualini

2527 **Transplantation of bovine adrenocortical cells encapsulated in alginate**
Mariya Balyura, Evgeny Gelfgat, Monika Ehrhart-Bornstein, Barbara Ludwig, Zohar Gendler, Uriel Barkai, Baruch Zimmerman, Avi Rotem, Norman L. Block, Andrew V. Schally, and Stefan R. Bornstein

MICROBIOLOGY

E871 **Dysregulation of *Escherichia coli* α -hemolysin expression alters the course of acute and persistent urinary tract infection**
Kanna Nagamatsu, Thomas J. Hannan, Randi L. Guest, Maria Kostakioti, Maria Hadjifrangiskou, Jana Binkley, Karen Dodson, Tracy L. Raivio, and Scott J. Hultgren

NEUROSCIENCE

E881 **Contribution of reactive oxygen species to cerebral amyloid angiopathy, vasomotor dysfunction, and microhemorrhage in aged Tg2576 mice**
Byung Hee Han, Meng-liang Zhou, Andrew W. Johnson, Itender Singh, Fan Liao, Ananth K. Vellimana, James W. Nelson, Eric Milner, John R. Cirrito, Jacob Basak, Min Yoo, Hans H. Dietrich, David M. Holtzman, and Gregory Joseph Zipfel

2533 **Critical and maximally informative encoding between neural populations in the retina**
David B. Kastner, Stephen A. Baccus, and Tatyana O. Sharpee

2539 **Belief about nicotine selectively modulates value and reward prediction error signals in smokers**
Xiaosi Gu, Terry Lohrenz, Ramiro Salas, Philip R. Baldwin, Alireza Soltani, Ulrich Kirk, Paul M. Cinciripini, and P. Read Montague
→ See Commentary on page 2301

2545 **Feedback stabilizes propagation of synchronous spiking in cortical neural networks**
Samat Moldakarimov, Maxim Bazhenov, and Terrence J. Sejnowski

2551 **Autism-associated mutation inhibits protein kinase C-mediated neuroligin-4X enhancement of excitatory synapses**
Michael A. Bembem, Quynh-Anh Nguyen, Tongguang Wang, Yan Li, Roger A. Nicoll, and Katherine W. Roche

2557 **Brain 5-HT deficiency increases stress vulnerability and impairs antidepressant responses following psychosocial stress**
Benjamin D. Sachs, Jason R. Ni, and Marc G. Caron

2563 **Metabolic resting-state brain networks in health and disease**
Phoebe G. Spetsieris, Ji Hyun Ko, Chris C. Tang, Amir Nazem, Wataru Sako, Shichun Peng, Yilong Ma, Vijay Dhawan, and David Eidelberg

2569 **Oxalic acid and diacylglycerol 36:3 are cross-species markers of sleep debt**
Aalim M. Weljie, Peter Meerlo, Namni Goel, Arjun Sengupta, Matthew S. Kayser, Ted Abel, Morris J. Birnbaum, David F. Dinges, and Amita Sehgal

2575 **Etiology of distinct membrane excitability in pre- and posthearing auditory neurons relies on activity of Cl⁻ channel TMEM16A**
Xiao-Dong Zhang, Jeong-Han Lee, Ping Lv, Wei Chun Chen, Hyo Jeong Kim, Dongguang Wei, Wenying Wang, Choong-Ryool Sihm, Karen Jo Doyle, Jason R. Rock, Nipavan Chiamvimonvat, and Ebenezer N. Yamoah

2581 Neuroinflammation triggered by β -glucan/dectin-1 signaling enables CNS axon regeneration

Katherine T. Baldwin, Kevin S. Carbajal, Benjamin M. Segal, and Roman J. Giger

2587 Gustatory and metabolic perception of nutrient stress in *Drosophila*

Nancy J. Linford, Jennifer Ro, Brian Y. Chung, and Scott D. Pletcher

2593 Elevated intraocular pressure decreases response sensitivity of inner retinal neurons in experimental glaucoma mice

Ji-Jie Pang, Benjamin J. Frankfort, Ronald L. Gross, and Samuel M. Wu

PHARMACOLOGY

E891 MmTX1 and MmTX2 from coral snake venom potently modulate GABA_A receptor activity

Jean-Pierre Rosso, Jürgen R. Schwarz, Marcelo Diaz-Bustamante, Brigitte Céard, José M. Gutiérrez, Matthias Kneussel, Olaf Pongs, Frank Bosmans, and Pierre E. Bougis

PHYSIOLOGY

2320 Lack of exercise leads to significant and reversible loss of scale invariance in both aged and young mice

Changgui Gu, Claudia P. Coomans, Kun Hu, Frank A. J. L. Scheer, H. Eugene Stanley, and Johanna H. Meijer

2599 SLO3 auxiliary subunit LRRC52 controls gating of sperm KSPER currents and is critical for normal fertility

Xu-Hui Zeng, Chengtao Yang, Xiao-Ming Xia, Min Liu, and Christopher J. Lingle

PLANT BIOLOGY

E901 FT-like proteins induce transposon silencing in the shoot apex during floral induction in rice

Shojiro Tamaki, Hiroyuki Tsuji, Ayana Matsumoto, Akiko Fujita, Zenpei Shimatani, Rie Terada, Tomoaki Sakamoto, Tetsuya Kurata, and Ko Shimamoto

E911 Structure, variation, and assembly of the root-associated microbiomes of rice



Joseph Edwards, Cameron Johnson, Christian Santos-Medellín, Eugene Lurie, Natraj Kumar Podishetty, Srijak Bhatnagar, Jonathan A. Eisen, and Venkatesan Sundaresan

→ See Commentary on page 2299

PSYCHOLOGICAL AND COGNITIVE SCIENCES

2389 Human language reveals a universal positivity bias



Peter Sheridan Dodds, Eric M. Clark, Suma Desu, Morgan R. Frank, Andrew J. Reagan, Jake Ryland Williams, Lewis Mitchell, Kameron Decker Harris, Isabel M. Kloumann, James P. Bagrow, Karine Megerdooian, Matthew T. McMahon, Brian F. Tivnan, and Christopher M. Danforth

2605 Coincidence avoidance principle in surface haptic interpretation

Steven G. Manuel, Roberta L. Klatzky, Michael A. Peshkin, and James Edward Colgate

SYSTEMS BIOLOGY

2337 Efficient solar-to-fuels production from a hybrid microbial–water-splitting catalyst system



Joseph P. Torella, Christopher J. Gagliardi, Janice S. Chen, D. Kwabena Bediako, Brendan Colón, Jeffery C. Way, Pamela A. Silver, and Daniel G. Nocera

2611 Greedy scheduling of cellular self-replication leads to optimal doubling times with a log-Frechet distribution



Rami Pugatch

2617 Metabolic theory predicts whole-ecosystem properties

John R. Schramski, Anthony I. Dell, John M. Grady, Richard M. Sibly, and James H. Brown

→ See Commentary on page 2303

CORRECTIONS (ONLINE ONLY)

CHEMISTRY

E921 Metal-free organic sensitizers for use in water-splitting dye-sensitized photoelectrochemical cells

John R. Swierk, Dalvin D. Méndez-Hernández, Nicholas S. McCool, Paul Liddell, Yuichi Terazono, Ian Pahk, John J. Tomlin, Nolan V. Oster, Thomas A. Moore, Ana L. Moore, Devens Gust, and Thomas E. Mallouk

PSYCHOLOGICAL AND COGNITIVE SCIENCES

E922 Mapping the unconscious maintenance of a lost first language

Lara J. Pierce, Denise Klein, Jen-Kai Chen, Audrey Delcenserie, and Fred Genesee

ix Subscription Form