

nature

biotechnology

THE SCIENCE AND BUSINESS OF BIOTECHNOLOGY

VOLUME 31 NUMBER 2 FEBRUARY 2013

www.nature.com/naturebiotechnology



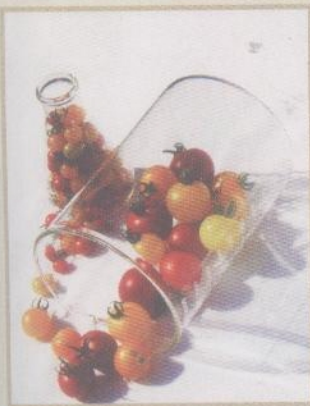
The epigenomics of fruit ripening
Sequencing human antibody repertoires
Small RNAs for metabolic engineering

5

0

1

nature biotechnology



Cherry and currant tomatoes of varying ripeness. Zhong *et al.* use whole-genome cytosine methylation and transcription factor binding analyses to show that epigenome dynamics influence the developmental transition to ripening (p 154).
Credit: Ryan McQuinn



Amgen buys gene hunter deCODE, p 87

EDITORIAL

- 85 Dishing out cancer treatment

NEWS

- 87 Amgen punts on deCODE's genetics know-how
- 88 Chinese investors tap US biotech
- 89 First novel anti-tuberculosis drug in 40 years
- 90 Citizen microbiome
- 90 Gilead widens cancer focus
- 91 Isis inks two antisense deals
- 91 Forty fight rust and rot
- 92 Exelixis debuts in rare cancer
- 92 First drug for short-bowel
- 92 Startups, inventors cheer European unified patent
- 93 Egg-free flu vaccines
- 93 UK science's Christmas gift
- 94 BioTime acquires Geron's stem cell program
- 94 Brüstle patent holds up in Germany
- 95 Industry backs biocatalysis for greener manufacturing
- 97 All conflicts of interest in one site
- 97 Around the world in a month
- 98 EDITOR'S PICK: Inovio
- 99 DATA PAGE: 2012—Bullish for big biotech
- 100 NEWS FEATURE: Fresh from the biotech pipeline—2012



BIOENTREPRENEUR

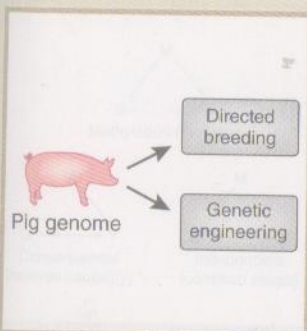
BUILDING A BUSINESS

- 104 Giving voice to India's entrepreneurs
Gayatri Saberwal



nature publishing group

Nature Biotechnology (ISSN 1087-0156) is published monthly by Nature Publishing Group, a trading name of Nature America Inc. located at 75 Varick Street, Fl 9, New York, NY 10013-1917. Periodicals postage paid at New York, NY and additional mailing post offices. **Editorial Office:** 75 Varick Street, Fl 9, New York, NY 10013-1917. Tel: (212) 726-9335, Fax: (212) 696-9753. **Annual subscription rates:** USA/Canada: US\$250 (personal), US\$4,677 (institution), US\$5,382 (corporate institution). Canada add 5% GST #104911595RT001; Euro-zone: €202 (personal), €3,713 (institution), €4,634 (corporate institution); Rest of world (excluding China, Japan, Korea): £130 (personal), £2,400 (institution), £2,990 (corporate institution); Japan: Contact NPG Nature Asia-Pacific, Chiyoda Building, 2-37 Ichigayatamachi, Shinjuku-ku, Tokyo 162-0843. Tel: 81 (03) 3267 8751, Fax: 81 (03) 3267 8746. **POSTMASTER:** Send address changes to *Nature Biotechnology*, Subscriptions Department, 75 Varick Street, 9th Floor, New York, NY 10013-1917. **Authorization to photocopy** material for internal or personal use, or internal or personal use of specific clients, is granted by Nature Publishing Group to libraries and others registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided the relevant copyright fee is paid direct to CCC, 222 Rosewood Drive, Danvers, MA 01923, USA. Identification code for *Nature Biotechnology*: 1087-0156/04. **Back issues:** US\$45, Canada add 7% for GST. CPC PUB AGREEMENT #40032744. Printed by Publishers Press, Inc., Lebanon Junction, KY, USA. Copyright © 2013 Nature America, Inc. All rights reserved. Printed in USA.



Swine reference genome, p 122

OPINION AND COMMENT

CORRESPONDENCE

- 108 Prize-based contests can provide solutions to computational biology problems**
Karim R Lakhani, Kevin J Boudreau, Po-Ru Loh, Lars Backstrom, Carliss Baldwin, Eric Lonstein, Mike Lydo, Alan MacCormack, Ramy A Arnaout & Eva C Guinan
- 111 Commercialized transgenic traits, maize productivity and yield risk**
Guanming Shi, Jean-Paul Chavas & Joseph Lauer

COMMENTARY

- 115 CASE STUDY: Liquid refreshment**
Christopher Scott

FEATURE

PATENTS

- 116 Intellectual property rights and user facility agreements**
Francis Hane
- 118 Recent patent applications in polyethylene glycosylation**

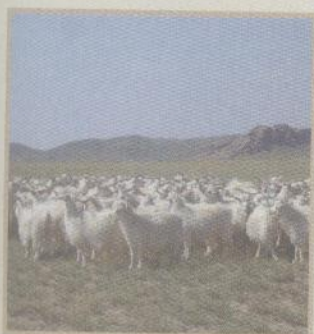
NEWS AND VIEWS

- 119 Epigenetic trigger for tomato ripening**
Joseph R Ecker **b** see also p 154
- 120 Discovery of antibiotic adjuvants**
Maya A Farha & Eric D Brown **b** see also p 160
- 122 Pig genomics for biomedicine**
Randall S Prather
- 123 Goat genome sequence by optical mapping**
H Craig Mak **b** see also p 135
- 125 Membrane channels built from DNA**
Markus Elsner
- 122 RESEARCH HIGHLIGHTS**

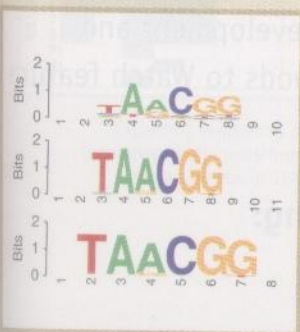
COMPUTATIONAL BIOLOGY

ANALYSIS

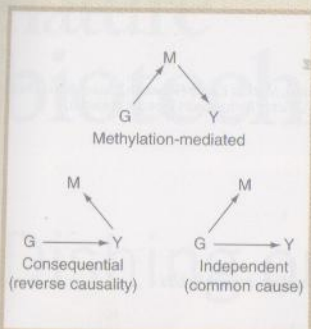
- 126 Evaluation of methods for modeling transcription factor sequence specificity**
Matthew T Weirauch, Atina Cote, Raquel Norel, Matti Annala, Yue Zhao, Todd R Riley, Julio Saez-Rodriguez, Thomas Cokelaer, Anastasia Vedenko, Shaheynoor Talukder, DREAM5 Consortium, Harmen J Bussemaker, Quaid D Morris, Martha L Bulyk, Gustavo Stolovitzky, Timothy R Hughes, Phaedra Agius, Aaron Arvey, Philipp Bucher, Curtis G Callan Jr, Cheng Wei Chang, Chien-Yu Chen, Yong-Syuan Chen, Yu-Wei Chu, Jan Grau, Ivo Grosse, Vidhya Jagannathan, Jens Keilwagen, Szymon M Kielbasa, Justin B Kinney, Holger Klein, Miron B Kursu, Harri Lähdesmäki, Kirsti Laurila, Chengwei Lei, Christina Leslie, Chaim Linhart, Anand Murugan, Alena Myšičková, William Stafford Noble, Matti Nykter, Yaron Orenstein, Stefan Posch, Jianhua Ruan, Witold R Rudnicki, Christoph D Schmid, Ron Shamir, Wing-Kin Sung, Martin Vingron & Zhizhuo Zhang



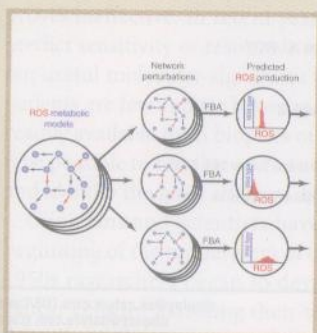
Optical mapping extends scaffolds of goat genome, p 123



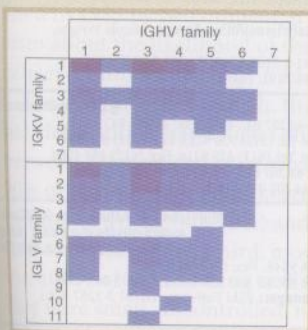
Benchmarking algorithms that model protein-DNA binding specificity, p 126



Linking epigenetics to disease, p 142



Strategy to identify targets for antibiotic adjuvants, p 160



Extracting sequences of immunoglobulin pairs from human B cells, p 166

RESEARCH

ARTICLES

- 135 Sequencing and automated whole-genome optical mapping of the genome of a domestic goat (*Capra hircus*)** **OPEN**
Yang Dong, Min Xie, Yu Jiang, Nianqing Xiao, Xiaoyong Du, Wenguang Zhang, Gwenola Tosser-Klopp, Jinhuan Wang, Shuang Yang, Jie Liang, Wenbin Chen, Jing Chen, Peng Zeng, Yong Hou, Chao Bian, Shengkai Pan, Yuxiang Li, Xin Liu, Wenliang Wang, Bertrand Servin, Brian Sayre, Bin Zhu, Deacon Sweeney, Rich Moore, Wenhui Nie, Yongyi Shen, Ruoping Zhao, Guojie Zhang, Jinquan Li, Thomas Faraut, James Womack, Yaping Zhang, James Kijas, Noelle Cockett, Xun Xu, Shuhong Zhao, Jun Wang & Wen Wang **1** see also p 123
- 142 Epigenome-wide association data implicate DNA methylation as an intermediary of genetic risk in rheumatoid arthritis**
Yun Liu, Martin J Aryee, Leonid Padyukov, M Daniele Fallin, Espen Hesselberg, Arni Runarsson, Lovisa Reinius, Nathalie Acevedo, Margaret Taub, Marcus Ronninger, Klementy Shchetynsky, Annika Scheynius, Juha Kere, Lars Alfredsson, Lars Klareskog, Tomas J Ekström & Andrew P Feinberg
- 148 Targeted zwitterionic near-infrared fluorophores for improved optical imaging**
Hak Soo Choi, Summer L Gibbs, Jeong Heon Lee, Soon Hee Kim, Yoshitomo Ashitate, Fangbing Liu, Hoon Hyun, GwangLi Park, Yang Xie, Soochan Bae, Maged Henary & John V Frangioni
- 154 Single-base resolution methylomes of tomato fruit development reveal epigenome modifications associated with ripening**
Silin Zhong, Zhangjun Fei, Yun-Ru Chen, Yi Zheng, Mingyun Huang, Julia Vrebalov, Ryan McQuinn, Nigel Gapper, Bao Liu, Jenny Xiang, Ying Shao & James J Giovannoni **1** see also p 119

LETTERS

- 160 Potentiating antibacterial activity by predictably enhancing endogenous microbial ROS production**
Mark P Brynildsen, Jonathan A Winkler, Catherine S Spina, I Cody MacDonald & James J Collins **1** see also p 120
- 166 High-throughput sequencing of the paired human immunoglobulin heavy and light chain repertoire**
Brandon J DeKosky, Gregory C Ippolito, Ryan P Deschner, Jason J Lavinder, Yariv Wine, Brandon M Rawlings, Navin Varadarajan, Claudia Giesecke, Thomas Dörner, Sarah F Andrews, Patrick C Wilson, Scott P Hunicke-Smith, C Grant Willson, Andrew D Ellington & George Georgiou
- 170 Metabolic engineering of *Escherichia coli* using synthetic small regulatory RNAs**
Dokyun Na, Seung Min Yoo, Hannah Chung, Hyegwon Park, Jin Hwan Park & Sang Yup Lee

CAREERS AND RECRUITMENT

- 175 Fourth-quarter biotech job picture**
- 176 PEOPLE**