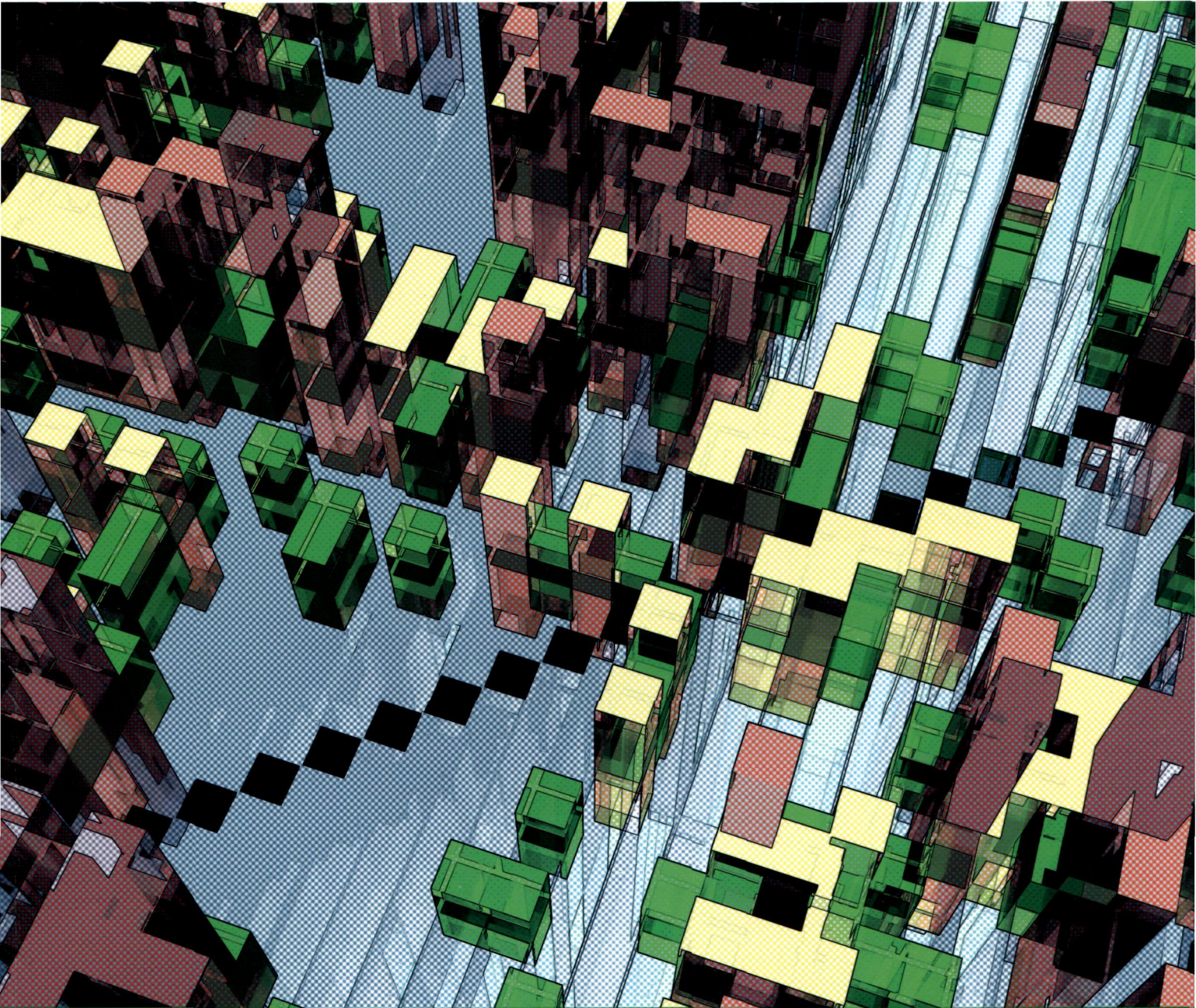


# Nature

## REVIEWS

January 2014 volume 15 no. 1  
[www.nature.com/reviews](http://www.nature.com/reviews)

# GENETICS

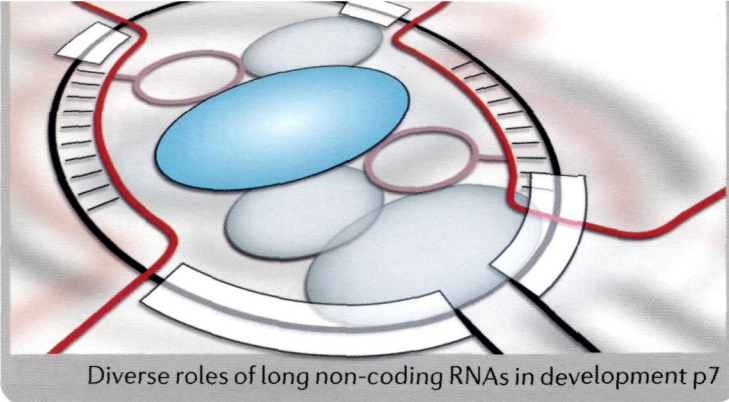


### PERVASIVE EPISTASIS

Insights from studies of complex traits in model organisms

### Clinical bacterial sequencing

Bioinformatic challenges



Diverse roles of long non-coding RNAs in development p7

# CONTENTS

January 2014  
volume 15 no. 1

## REVIEWS

### 7 Long non-coding RNAs: new players in cell differentiation and development



Alessandro Fatica and Irene Bozzoni

Our knowledge of the diverse types and roles of long non-coding RNAs (lncRNAs) is rapidly increasing. This Review discusses our latest understanding of lncRNAs that have validated functional roles in various differentiation and developmental processes.

### 22 Epistasis and quantitative traits: using model organisms to study gene–gene interactions

FEATURED ARTICLE

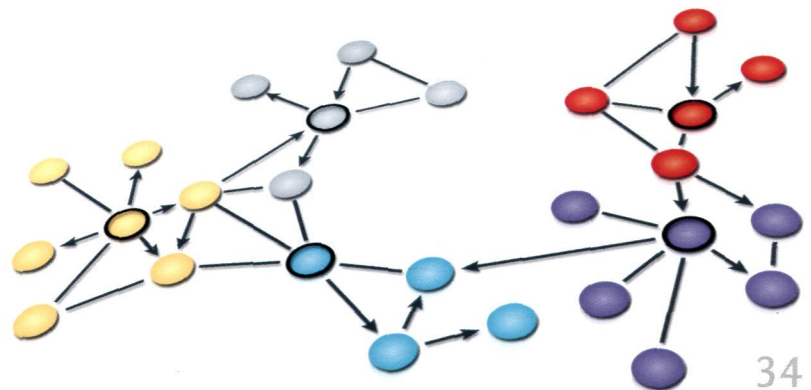
Trudy F. C. Mackay

The role of epistasis in quantitative traits is controversial. This Review argues that findings from studies of these traits are consistent with pervasive epistasis and discusses how experimental designs in model organisms are used to uncover the underlying genetic interactions.

### 34 Systems genetics approaches to understand complex traits

Mete Civelek and Aldons J. Lusis

Complex organismal traits, including diseases, are controlled by intricate interactions between multiple genes, intermediate molecular and cellular phenotypes, and environmental influences. This Review describes how systems genetics integrates these layers of information to provide a cohesive understanding of the molecular underpinnings of complex traits.



### On the web [www.nature.com/reviews/genetics](http://www.nature.com/reviews/genetics)

#### Advance online publication

We operate an advance online publication (AOP) service for authors and readers to view the latest articles published online ahead of print.

#### Forthcoming articles:

Chromatin modifiers and remodellers: regulators of cellular differentiation  
Taiping Chen and Sharon Y. R. Dent

Dynamic regulation of transcriptional states by chromatin and transcription factors

Ty C. Voss and Gordon L. Hager

Nature Reviews Genetics (ISSN 1471-0056) is published monthly by Nature Publishing Group, a division of Macmillan Publishers Ltd, The Macmillan Building, 4 Crinan Street, London N1 9XW, UK. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form (electronic or otherwise) without prior permission from [permissions@nature.com](mailto:permissions@nature.com). US Periodicals postage paid at Jamaica, NY, and additional mailing post offices. US POSTMASTER: Send address changes to Nature Publishing Group, Air Business Ltd, c/o Worldnet Shipping Inc., 156-15, 146th Avenue, 2nd Floor, Jamaica, NY 11434, USA.  
© 2014 Macmillan Publishers Limited. All rights reserved. Printed in United Kingdom.

### SERIES ON NON-CODING RNA

<http://www.nature.com/nrg/series/noncoding>

### SERIES ON APPLICATIONS OF NEXT-GENERATION SEQUENCING

<http://www.nature.com/nrg/series/nextgeneration>

**Key points** provides a bullet-pointed summary of the main topics covered in each article.

#### Links to further information

The full text of articles includes author biographies, links to glossary terms and links to websites and databases with relevant information.

#### Twitter

Follow [Nature Reviews Genetics](#) on Twitter for the latest news from the journal and beyond.

## RESEARCH HIGHLIGHTS

1 Selections from the recent scientific literature

## ETHICS WATCH

6 A big step for Finnish biobanking  
*Joanna Stjernaschantz Forsberg and Sirpa Soini*

## PERSPECTIVES


OPINION

49  **Bacterial genome sequencing in the clinic: bioinformatic challenges and solutions**

*W. Florian Fricke and David A. Rasko*

Bacterial whole-genome sequencing is showing promise in clinical applications. Here, the authors present their opinions on what the main bioinformatic challenges are in transferring bacterial whole-genome sequencing to medical diagnostics.

OPINION

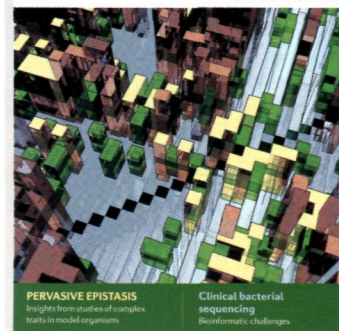
56  **The role of replicates for error mitigation in next-generation sequencing**

*Kimberly Robasky, Nathan E. Lewis and George M. Church*

Next-generation sequencing for variant identification is now becoming widespread, although pipelines have not yet been optimized. In this Perspective article, the authors discuss ways to minimize erroneous variant calls, in particular, by using replicates.

62 **Advanced genetic tools for plant biotechnology (corrigendum)**

*Wusheng Liu, Joshua S. Yuan and C. Neal Stewart Jr*



**PERSVASIVE EPISTASIS**  
Insights from studies of complex traits in model organisms

**Clinical bacterial sequencing**  
Bioinformatic challenges

► **COVER:** 'Falls into place' by Patrick Morgan, inspired by the Review on p22.



A big step for Finnish biobanking p6

### EDITORIAL & PRODUCTION OFFICE

The Macmillan Building, 4 Crinan Street, London N1 9XW, UK  
Tel: +44 (0)20 7843 3620  
Email: [NatureReviews@nature.com](mailto:NatureReviews@nature.com)  
[www.nature.com/reviews/genetics](http://www.nature.com/reviews/genetics)

**CHIEF EDITOR** Louisa Flintoft  
**SENIOR EDITOR** Mary Muers  
**ASSOCIATE EDITORS** Hannah Stower, Darren Burgess  
**ASSISTANT EDITOR** Isabel Lokody  
**COPY EDITOR** Esther Lau  
**SENIOR ART EDITOR (NRG)** Patrick Morgan  
**COPY EDITING MANAGER** Catriona Rodwell  
**SENIOR COPY EDITOR** Mariam Faruqi  
**SENIOR EDITORIAL ASSISTANT** Laura Corns  
**EDITORIAL ASSISTANT** Emily Finn  
**MANAGING PRODUCTION EDITOR** Judith Shadwell  
**SENIOR PRODUCTION EDITOR** Simon Fenwick  
**ART CONTROLLER** Susanne Harris  
**SENIOR ART EDITOR** Vicky Summersby  
**PRODUCTION CONTROLLER** Natalie Smith  
**MANAGING EDITOR** Suzanne Farley  
**PUBLISHER** Alison Mitchell

**CUSTOMER SERVICES** [www.nature.com/help](http://www.nature.com/help)  
**PERSONAL SUBSCRIPTIONS** [subscriptions@nature.com](mailto:subscriptions@nature.com)  
**REPRINTS** [www.nature.com/reprints](http://www.nature.com/reprints)  
**ADVERTISING & SPONSORSHIP**  
[www.nature.com/advertising](http://www.nature.com/advertising)  
**SITE LICENCES**  
[www.nature.com/libraries/site\\_licences/index.html](http://www.nature.com/libraries/site_licences/index.html)  
**PRESS OFFICE** [press@nature.com](mailto:press@nature.com)  
**MARKETING** [marketing@nature.com](mailto:marketing@nature.com)

### MANAGEMENT OFFICES

**NPG LONDON** The Macmillan Building, 4 Crinan Street, London N1 9XW, UK. Tel: +44 (0)20 7833 4000  
**NPG NEW YORK** 75 Varick Street, 9th floor, New York, NY 10013-1917, USA. Tel: +1 212 726 9200  
**NPG ASIA-PACIFIC** Chiyoda Building 2-37 Ichigayatamachi, Shinjuku-Ku, Tokyo 16200843, Japan. Tel: +1 212 726 9200  
A list of other offices can be found at [www.nature.com/npg/contact/offices.html](http://www.nature.com/npg/contact/offices.html)

Copyright © 2014 Nature Publishing Group  
Printed in Wales by Cambrian Printers on acid-free paper.

### EDITORS



LOUISA FLINTOFT



MARY MUERS



HANNAH STOWER



DARREN BURGESS



ISABEL LOKODY