



nature publishing group

nature
REVIEWSNovember 2011 Volume 12 No. 11
www.nature.com/reviews

GENETICS

TESTS FOR ADAPTATION
How to be certain that alleles
affect fitnessType 1 diabetes
A genetic and functional understanding
of susceptibility genes

► **COVER:** 'Semblance' by Patrick Morgan, inspired by the Review on p767.



LOUISA FLINTOFT



TANITA CASCI



MARY MUERS



DARREN BURGESS

In the words of Ernst Mayr, “mutation is the ultimate source of all genetic variation”. And yet, as illustrated by several articles in this issue, much is still to be learnt about where and how mutations occur.

A genome is not a level playing field when it comes to mutation. Hodgkinson and Eyre-Walker (Review, p756) discuss insights from comparative genomics into how mutation rates vary across mammalian genomes. The emerging picture is of a complex range of influences on mutation rate — from neighbouring nucleotides to whole-chromosome effects — but, in many cases, the molecular basis remains poorly understood. A better understanding of regions of the genome that are particularly susceptible to mutation may be useful for studies of disease and adaptation.

Indeed, the data that are being produced by exome sequencing — strategies for which are discussed in a Review by Bamshad and colleagues (p745) — will provide a wealth of information on the distribution of protein-coding mutations. An average exome from an African American yields ~24,000 single-nucleotide variants, and resequencing gives the opportunity to identify rare as well as common events.

Also, a Research Highlight on p741 explains a new strategy for genome-wide mapping of another type of mutation — translocation. And another Research Highlight (p740) suggests that we will need to broaden our horizons when considering mutations to include epimutations: DNA methylation changes that are carried across generations.

Finally, the print copy of this issue is accompanied by a free Poster by Chang and Hannon on ‘Tools for understanding and using small RNAs: from pathways to functions to therapies’. This Poster is also available free [online](#) and has been produced with kind support from Thermo Scientific.

EDITORIAL OFFICES

LONDON NatureReviews@nature.com
The Macmillan Building,
4 Crinan Street, London N1 9XW, UK
Tel: +44 (0)20 7843 3620;
Fax: +44 (0)20 7843 3629

CHIEF EDITOR: Louisa Flintoft
SENIOR EDITORS: Tanita Casci, Mary Muers
ASSISTANT EDITOR: Darren Burgess
COPY EDITOR: Matthew Smyllie
SENIOR COPY EDITORS: Yukie Ozawa,
Catriona Rodwell, Man Tsuey Tse, Lucie Wootton
COPY EDITING MANAGER: Lewis Packwood
SENIOR ART EDITOR (NRG): Patrick Morgan
ART CONTROLLER: Susanne Harris
SENIOR ART EDITORS: Vicky Summersby,
Kirsten Lee
MANAGING PRODUCTION EDITOR:
Judith Shadwell
SENIOR PRODUCTION EDITOR:
Simon Fenwick
PRODUCTION CONTROLLER: Natalie Smith

SENIOR EDITORIAL ASSISTANT: Laura Corns
EDITORIAL ASSISTANT: Ella Lines
WEB PRODUCTION MANAGER: Deborah Anthony
MARKETING MANAGERS: Tim Redding,
Leah Rodriguez

MANAGEMENT OFFICES

LONDON nature@nature.com
The Macmillan Building, 4 Crinan Street,
London N1 9XW, UK
Tel: +44 (0)20 7833 4000;
Fax: +44 (0)20 7843 4596/7
OFFICE MANAGER: Laura Lee
MANAGING EDITOR: Suzanne Farley
PUBLISHER: James Butcher
MANAGING DIRECTOR:
Steven Inchcoombe
EDITOR-IN-CHIEF, NATURE PUBLICATIONS:
Philip Campbell
ASSOCIATE DIRECTORS: Jenny Henderson,
Dominic Pettit
EDITORIAL PRODUCTION DIRECTOR:
James McQuat

PRODUCTION DIRECTOR:
Yvonne Strong
DIRECTOR, WEB PUBLISHING:
Dan Pollock
HEAD OF WEB PRODUCTION:
Alexander Thurrell

NEW YORK nature@natureny.com
Nature Publishing Group,
75 Varick Street, 9th floor, New York,
NY 10013-1917, USA
Tel: +1 212 726 9200;
Fax: +1 212 696 9006

CHIEF TECHNOLOGY OFFICER:
Howard Ratner
HEAD OF INTERNAL SYSTEMS DEVELOPMENT:
Anthony Barrera
HEAD OF SOFTWARE SERVICES:
Luigi Squillante
**GLOBAL HEAD OF ADVERTISING AND
SPONSORSHIP:** Dean Sanderson
**HEAD OF NATURE RESEARCH & REVIEWS
MARKETING:** Sara Girard

TOKYO nature@natureasia.com
Chiyoda Building 5F, 2-37-1 Ichigayatamachi,
Shinjuku-ku, Tokyo 162-0843, Japan
Tel: +81 3 3267 8751; Fax: +81 3 3267 8746
ASIA-PACIFIC PUBLISHER: Antoine E. Bocquet
MANAGER: Koichi Nakamura
ASIA-PACIFIC SALES DIRECTOR:
Kate Yoneyama
SENIOR MARKETING MANAGER:
Peter Yoshihara
MARKETING/PRODUCTION MANAGER:
Takesh Murakami
INDIA 5A/12 Ansari Road, Daryaganj,
New Delhi 110 002, India
Tel/Fax: +91 11 2324 4186
SALES AND MARKETING MANAGER, INDIA:
Harpal Singh Gill

Copyright © 2011 Nature Publishing Group
Research Highlight images courtesy of
Getty Images unless otherwise credited.
Printed in Wales by Cambrian Printers
on acid-free paper