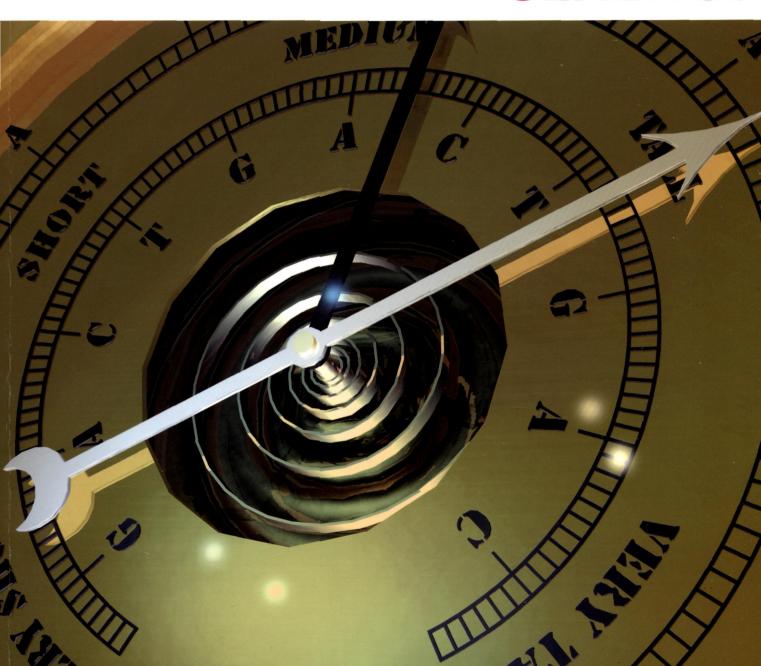


july 2013 volume 14 no. 7 www.nature.com/reviews

# **GENETICS**

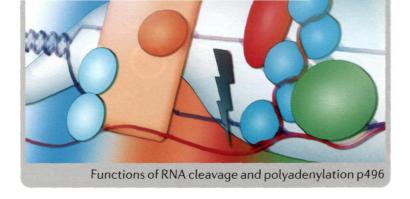


# PREDICTIVE POWER?

From SNP genotypes to complex trait phenotypes

Sequencing-based studies for disease-gene discovery

Optimizing design and interpretation



# CONTENTS July 2013 volume 14 no. 7

# REVIEWS

#### Argonaute proteins: functional insights and emerging roles



Gunter Meister

Argonaute proteins are vital components of small-RNA-quided modes of gene regulation. Recent studies have provided important details about classical modes of Argonaute function, such as their structure and loading with small RNAs, and have also revealed unexpected roles in other cellular functions.

#### Sequencing studies in human genetics: design and interpretation

David B. Goldstein, Andrew Allen, Jonathan Keebler, Elliott H. Margulies, Steven Petrou, Slavé Petrovski and Shamil Sunyaev

Next-generation sequencing is now poised for the discovery of genetic variants involved in common and rare diseases. Here, the authors present considerations for the workflow of these studies in order to identify true associations of disease and mutation.

#### Genomic and epigenetic insights into the molecular bases of heterosis

Z. Jeffrey Chen

Heterosis, also known as hybrid vigour, is an intriguing phenomenon that has particularly important implications for agriculture. The molecular basis of this vigour is poorly understood, but progress is being made through the use of genomic, transcriptomic and epigenomic approaches.

#### Pleiotropy in complex traits: challenges and strategies

Nadia Solovieff, Chris Cotsapas, Phil H. Lee, Shaun M. Purcell and Jordan W. Smoller

Modern genomic studies are revealing widespread associations between single genetic variants and multiple distinct traits, including diseases. This Review discusses the biological underpinnings of such pleiotropy and the available bioinformatic tools for the detection and characterization of these effects, as well as the implications for understanding human disease.

496 FEATURED ARTICLE

#### Alternative cleavage and polyadenylation: extent, regulation and function

Ran Elkon, Alejandro P. Ugalde and Reuven Agami Recent advances have allowed the genomic characterization of the extent and regulation of alternative polyadenylation. Here, the biological processes with which alternative polyadenylation has been associated, the mechanisms of its regulation and its involvement in disease are discussed.



M. Miller and D. K. Ko

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Eukaryotic transcriptional dynamics: from single molecules to cell populations Antoine Coulon, Carson C. Chow, Robert H. Singer and Daniel R. Larson

From promises to practical strategies in epigenetic epidemiology Jonathan Mill and Bastiaan T. Heijmans

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#### E-alert table of contents

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NATURE REVIEWS GENETICS





Research Highlight on forest tree genomics p444

### RESEARCH HIGHLIGHTS

441 Selections from the recent scientific literature

#### ETHICS WATCH

Forensic familial searching: scientific and social implications
Nanibaa' A. Garrison, Rori V. Rohlfs and Stephanie M. Fullerton

# **PERSPECTIVES**

OPINION

#### 507 Pitfalls of predicting complex traits from SNPs

Naomi R. Wray, Jian Yang, Ben J. Hayes, Alkes L. Price, Michael E. Goddard and Peter M. Visscher

The data from genome-wide association studies can be applied to genotype data to predict the phenotype of a complex trait. Here the authors discuss the potential pitfalls of such analyses and the inherent limitations of the method.



#### **EDITORIAL OFFICE**

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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

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