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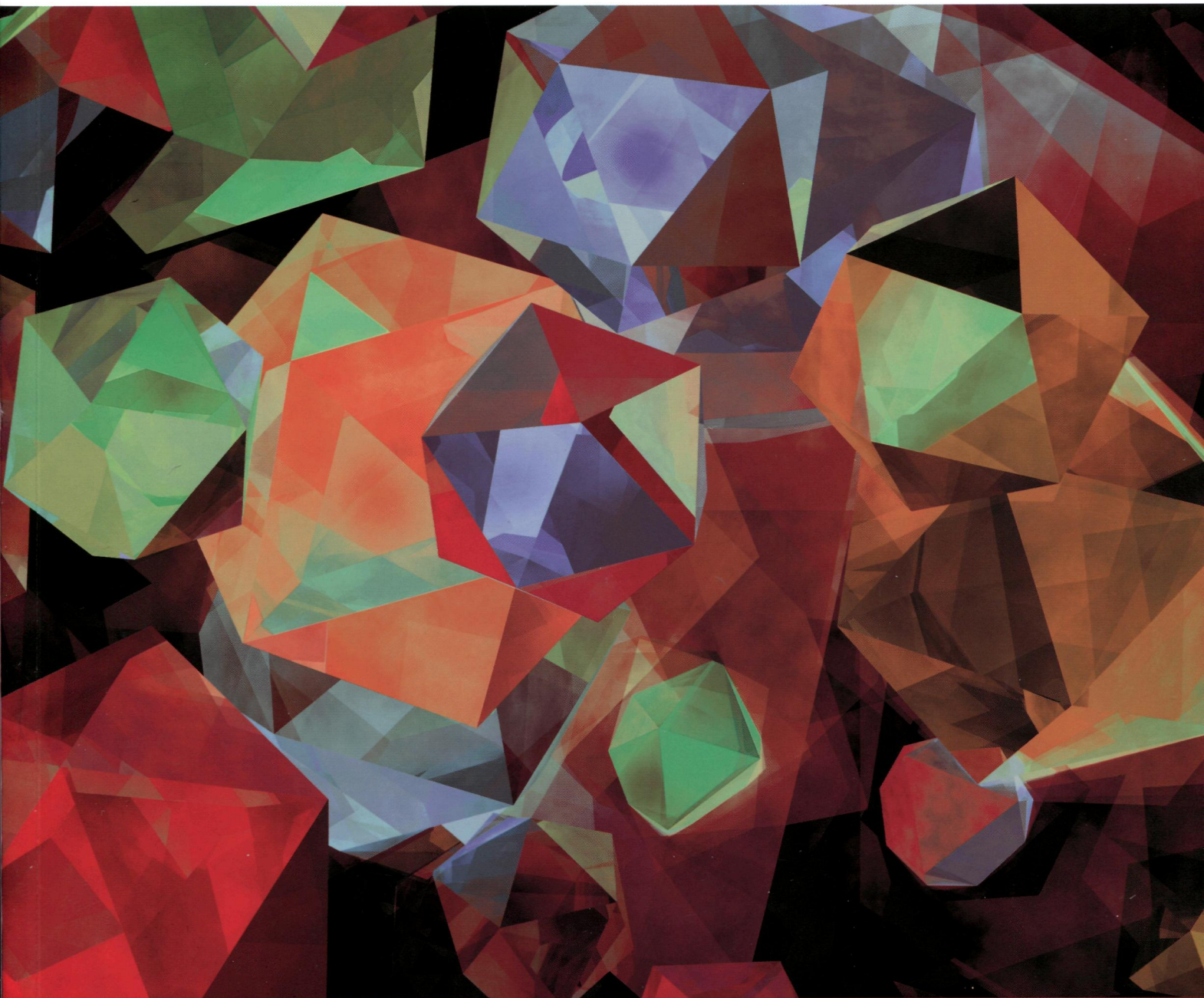
# Nature

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# REVIEWS

july 2014 volume 15 no. 7  
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## GENETICS



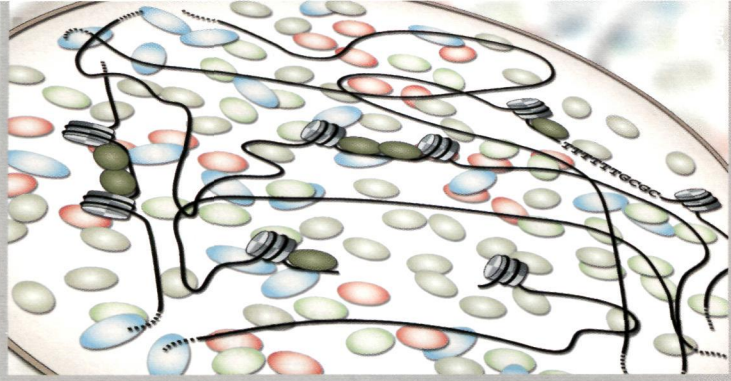
### MULTILAYERED CODE

Uncovering the regulatory information hidden in DNA

### Gene therapy in the clinic

Using genetics to optimize adeno-associated viral vectors





Diverse roles of telomeric components outside telomeres p491

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## REVIEWS

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### In pursuit of design principles of regulatory sequences

*Michal Levo and Eran Segal*

Gene-regulatory DNA elements control complex spatiotemporal patterns of gene expression, and alterations to these sequences are commonly associated with inter-individual phenotypic variation and human disease. This Review discusses our latest understanding of how different layers of information in these sequences control the binding of regulators and influence gene expression outcomes.

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FEATURED  
ARTICLE

### Insights into RNA structure and function from genome-wide studies

*Stefanie A. Mortimer, Mary Anne Kidwell and Jennifer A. Doudna*

Recent technological advances have enabled the probing of RNA structure across the transcriptomes of various species *in vitro* and *in vivo*. This Review discusses our latest understanding of how RNA structure influences various steps of gene expression, including translation, mRNA localization and microRNA-mediated gene regulation.

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### Empirical fitness landscapes and the predictability of evolution

*J. Arjan G. M. de Visser and Joachim Krug*

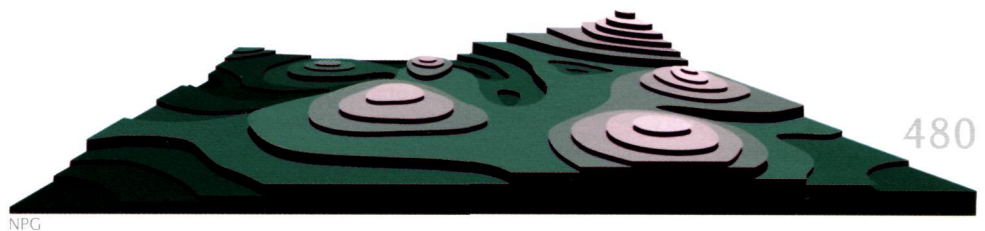
A central topic in biology concerns how genotypes determine phenotypes and functions of organisms that affect their evolutionary fitness. This Review discusses recent advances in the development of empirical fitness landscapes and their contribution to theoretical analyses of the predictability of evolution.

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### Transcriptional outcome of telomere signalling

*Jing Ye, Valérie M. Renault, Karine Jamet and Eric Gilson*

The role of telomeric factors as guardians of chromosome ends from threats to genome integrity (such as degradation and inappropriate DNA damage response activation) has long been appreciated. This Review discusses the extratelomeric activity of these factors and how they can regulate the transcription of genes involved in metabolism, immunity and differentiation.



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*Thomas Hellday, Saeed Eshtad and Serena Nik-Zainal*

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*Jo Peters*

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*Vera Gorbunova, Andrei Seluanov, Zhengdong Zhang, Vadim N. Gladyshev and Jan Vijg*

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Melissa A. Kotterman and David V. Schaffer

Although gene delivery vectors based on adeno-associated viruses (AAVs) have emerged as safe and effective for numerous clinical gene therapy applications, many challenges remain. Recent advances in AAV vector development through rational design and directed evolution, as well as in the design of novel genetic cargoes, promise to extend clinical successes of AAV-mediated gene therapy.

## PERSPECTIVES

OPINION

504 The dawn of evolutionary genome engineering

Csaba Pál, Balázs Papp and György Pósfai

In this Opinion article, the authors highlight the potential of genome engineering for the study of evolution and focus on microbial systems. They discuss the prospects and problems of the emerging field of evolutionary genome engineering, and pinpoint how a combination of genome engineering and laboratory evolution can shed light on evolutionary forces.



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