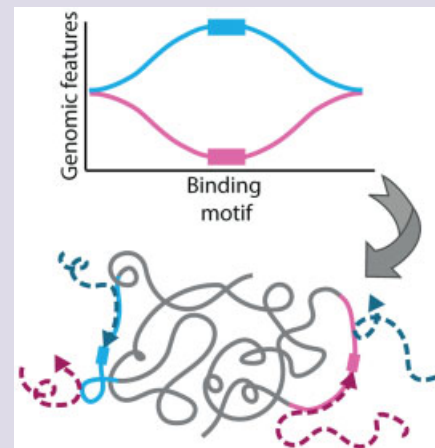


## Transcription factor binding: More than just motif recognition

On pages 605-612 Iris Dror et al. hypothesize that DNA recognition by a transcription factor (TF) is not only dependent on the respective DNA motif but is also influenced by the environment in which the motif resides. The authors argue that the environment may help to attract the TF to its binding site thus providing a more efficient search process. GC content and preferred DNA shape are two of the features playing an important role in that regard. In addition, homotypic clusters, i.e. the presence of multiple binding sites of the same TF, also contribute to TF binding. – kb

**Highlighted article:** How motif environment influences transcription factor search dynamics: Finding a needle in a haystack. Iris Dror et al. [dx.doi.org/10.1002/bies.201600005](https://doi.org/10.1002/bies.201600005)



## How YAP and TAZ respond to different cues

Ahmed Elbediwy et al. take a closer look at the regulation of YAP and TAZ in different mammalian epithelial tissues and at that of the corresponding *Drosophila* homologue Yorkie (see pages 644-653). The authors discuss how these transcriptional co-activators mainly act as sensors for cell polarity but are also able to respond to other signals, such as mechanical forces and tissue damage. In basal stem/progenitor cells YAP/TAZ is found in the nucleus and activated via Integrins and Scr family kinases. In differentiated squamous cells or columnar cells, on the other hand, they are retained in the cytoplasm and thus inhibited. This occurs via the canonical Hippo pathway. Furthermore, the authors also review the role of YAP/TAZ in human epithelial cancers. – kb

## Editorial

**Trading off accountability against professional survival? Or the consequences of Pareto's principle. . .**  
Andrew Moore ..... 587

## Thoughts & Opinion

### Correspondence

**How storytelling can help scientists to write better abstracts**  
Jacopo Marino ..... 590

## Primary Research

### Originals

**IRAK regulates macrophage foam cell formation by modulating genes involved in cholesterol uptake and efflux in cholesterol uptake and efflux**  
Minakshi Rana, Amit Kumar, Rajiv Lochan Tiwari, Vishal Singh, Tulika Chandra, Madhu Dikshit and Manoj Kumar Barthwal ..... 591

## Insights & Perspectives

### Hypotheses

**How motif environment influences transcription factor search dynamics: Finding a needle in a haystack**  
Iris Dror, Remo Rohs and Yael Mandel-Gutfreund ..... 605

### Ideas & Speculations

**How and why multiple MCMs are loaded at origins of DNA replication**  
Shankar P. Das and Nicholas Rhind .... 613

### Think again

**Cofactor squelching: Artifact or fact?**  
Søren Fisker Schmidt, Bjørk Ditlev Larsen, Anne Loft and Susanne Mandrup ..... 618

## Prospects & Overviews

### Review essays

**Bistability of mitotic entry and exit switches during open mitosis in mammalian cells**  
Nadia Hégarat, Scott Rata and Helfrid Hochegger ..... 627

**YAP and TAZ in epithelial stem cells: A sensor for cell polarity, mechanical forces and tissue damage**  
Ahmed Elbediwy, Zoé I. Vincent-Mistiaen and Barry J. Thompson ..... 644

**Lineage-specific genomics: Frequent birth and death in the human genome**  
Robert S. Young ..... 654

**Missing heritability of complex diseases: Enlightenment by genetic variants from intermediate phenotypes**  
Adrián Blanco-Gómez, Sonia Castillo-Lluva, María del Mar Sáez-Freire, Lourdes Hontecillas-Prieto, Jian Hua Mao, Andrés Castellanos-Martín, and Jesus Pérez-Losada ..... 664

**RNA assemblages orchestrate complex cellular processes**  
Finn Cilius Nielsen, Heidi Theil Hansen and Jan Christiansen ..... 674

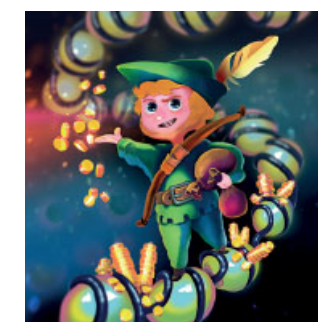
**Antibiotic resistance and virulence: Understanding the link and its consequences for prophylaxis and therapy**  
Thomas Guillard, Stéphanie Pons, Damien Roux, Gerald B. Pier and David Skurnik ..... 682

**Adaptation to nocturnality – learning from avian genomes**  
Diana Le Duc and Torsten Schöneberg ..... 694

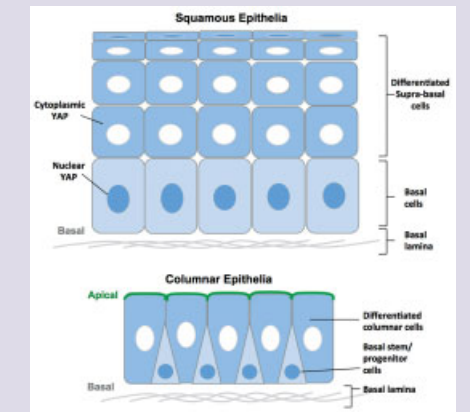
**Answering evolutionary questions: A guide for mechanistic biologists**  
Joanna Masel and Daniel E. L. Promislow ..... 704

### Problems & Paradigms

## Cover Photograph



On pages 618-626, Schmidt et al. discuss the concept of cofactor squelching in light of recent evidence from genome-wide studies indicating that such competition for a limiting amount of coactivators is a general mechanism of transcriptional repression by signal-dependent transcription factors (TFs). They further discuss how TF cooperativity in so-called hotspots and super-enhancers may sensitize these enhancers to cofactor squelching. The cover illustrates how signal dependent TFs can be regarded as the 'Robin Hoods' of the genome, redistributing cofactors (gold coins) from the wealthy super-enhancers (stacks of gold coins). Cover design: Andreas N. Grøntved.



## Is antibiotic resistance really associated with a fitness cost?

On pages 682-693, Thomas Guillard et al. critically review the long-held paradigm that "antibiotic resistance is usually associated with a fitness cost". Contrary to this paradigm, recent findings suggest that antibiotic-resistant bacterial strains might not only be fitter but also more virulent. The authors not only discuss the implications of these findings for the treatment of bacterial infections but also present alternative approaches, such as preventive and therapeutic anti-bacterial immunotherapies. – kb

**Highlighted article:** Antibiotic resistance and virulence: Understanding the link and its consequences for prophylaxis and therapy. Thomas Guillard et al. [dx.doi.org/10.1002/bies.201500180](https://doi.org/10.1002/bies.201500180)

