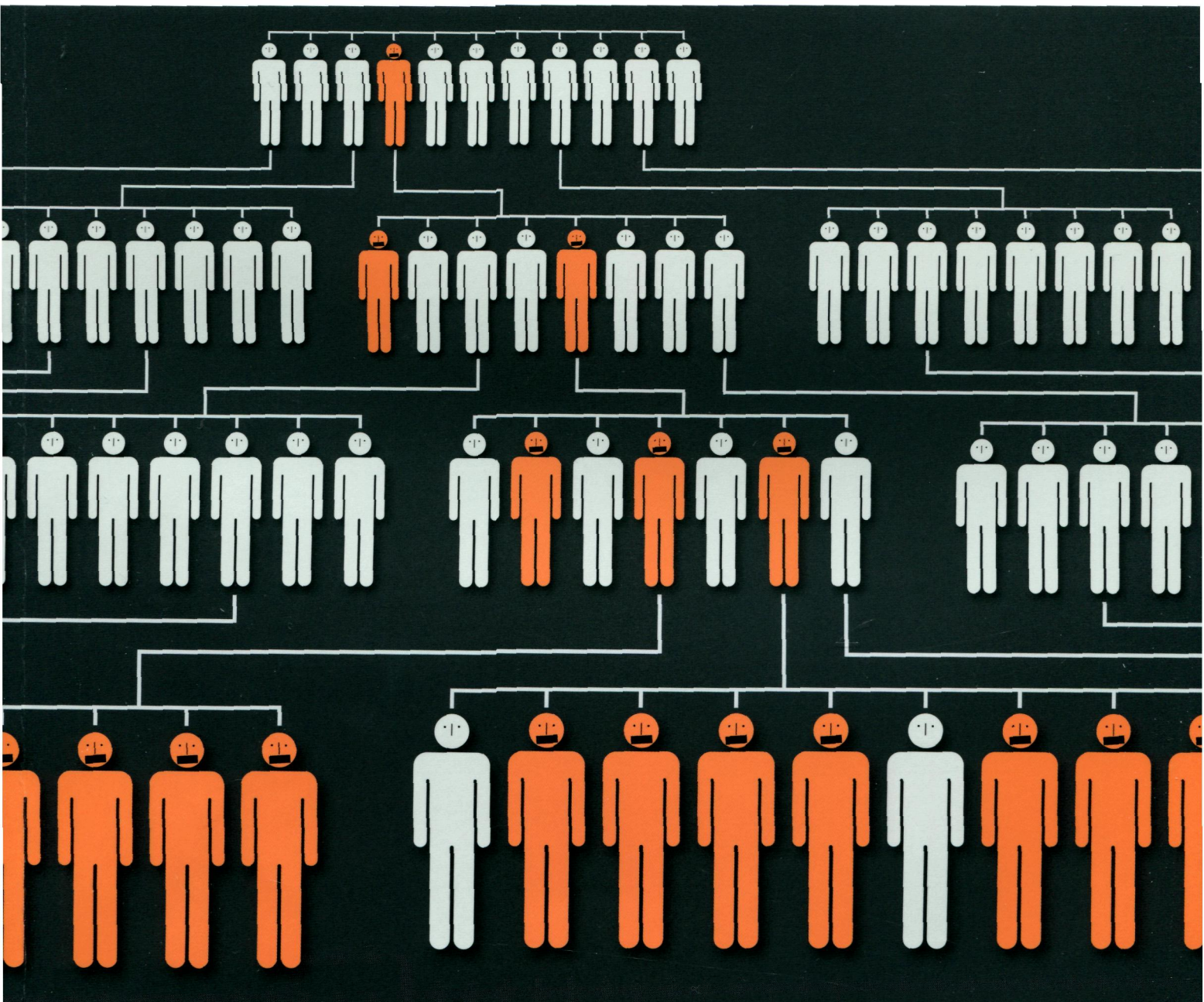


# nature

## REVIEWS

july 2013 volume 11 no. 7  
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# MICROBIOLOGY



### BEATING THE SILENT EPIDEMIC

Advanced antiviral therapy for HCV

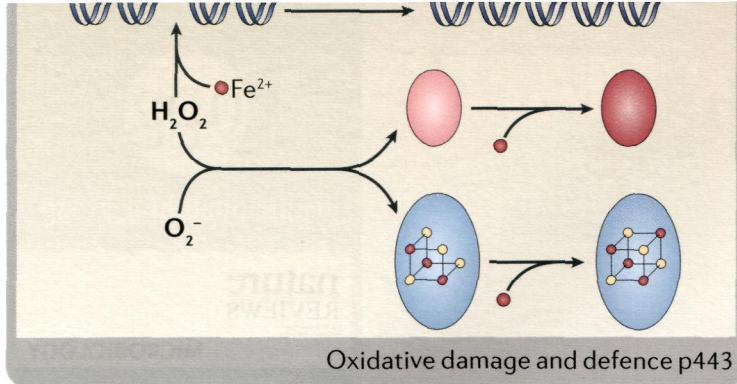
### Do the maths

Fulfilling the promise of  
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Oxidative damage and defence p443

## REVIEWS

### 443 The molecular mechanisms and physiological consequences of oxidative stress: lessons from a model bacterium

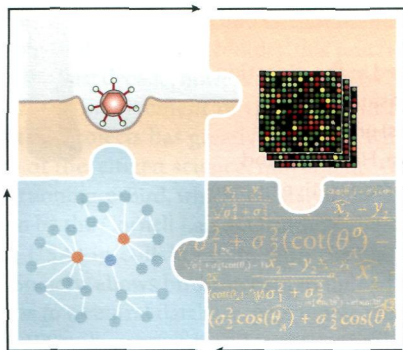
James A. Imlay

To survive in oxic environments, all organisms require mechanisms to degrade toxic reactive oxygen species (ROS). In this Review, James Imlay describes the oxidative stress response of *Escherichia coli* and considers the damage caused by ROS and the adaptive strategies used by this bacterium to minimize intracellular ROS accumulation.

### 455 Systems virology: host-directed approaches to viral pathogenesis and drug targeting

G. Lynn Law, Marcus J. Korth, Arndt G. Benecke and Michael G. Katze

Katze and colleagues provide an overview of the evolution of systems virology and the insights obtained from using such methodologies to study virus–host interactions. Combining systems, mathematical and computational approaches with traditional virology research will offer a better understanding of how viruses cause disease and will help in the development of therapeutics.



### 467 Fortifying the barrier: the impact of lipid A remodelling on bacterial pathogenesis

Brittany D. Needham and M. Stephen Trent

Lipid A is the bioactive component of the Gram-negative outer membrane and is extensively remodelled to enable the bacterium to subvert the immune system of the host. Here, Needham and Trent describe the regulation of lipid A-modifying enzymes, the host defences that target lipid A and the strategies that bacterial pathogens use to avoid immune detection.

### 482 The molecular and structural basis of advanced antiviral therapy for hepatitis C virus infection

FEATURED  
ARTICLE

Ralf Bartenschlager, Volker Lohmann and Francois Penin

Hepatitis C virus infection is a major cause of liver cirrhosis and cancer, and current therapies are often ineffective or have severe side effects. Here, Bartenschlager and colleagues review how structural and functional insights into the viral life cycle have allowed the development of novel direct-acting antiviral agents.

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Cyclic di-AMP: another second messenger enters the fray  
Rebecca M. Corrigan and Angelika Gründling

Molecular pathogenesis of the obligate intracellular bacterium *Coxiella burnetii*  
Erin J. van Schaik, Chen Chen, Katja Mertens, Mary M. Weber and James E. Samuel

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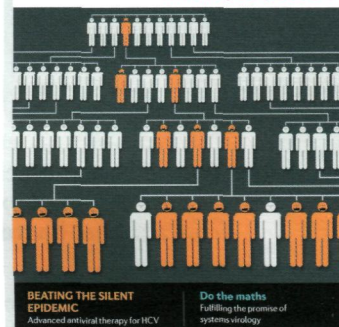


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REVIEWS

July 2013 Volume 11 No. 2  
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**MICROBIOLOGY**



**BEATING THE SILENT EPIDEMIC**  
Advanced antiviral therapy for HCV

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Fulfilling the promise of systems virology

► **COVER:** 'Silent epidemic' by Philip Patenall, inspired by the Review on p482.



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## PROGRESS

435 **Transposon insertion sequencing: a new tool for systems-level analysis of microorganisms**



*Tim van Opijnen and Andrew Camilli*

The combination of transposon mutagenesis with next-generation sequencing has emerged as a useful tool for identifying putative gene function in a high-throughput manner. Here, van Opijnen and Camilli describe the four main techniques that are used for this purpose, with a focus on their application for uncovering bacterial gene function.

## ANALYSIS

497 **The abundance and variety of carbohydrate-active enzymes in the human gut microbiota**

*Abdessamad El Kaoutari, Fabrice Armougom, Jeffrey I. Gordon, Didier Raoult and Bernard Henrissat*

The human genome encodes very few enzymes involved in the digestion of complex polysaccharides, and this deficit is compensated for by the myriad of carbohydrate-active enzymes (CAZymes) encoded by members of the gut microbiome. In this Analysis article, Henrissat and colleagues characterize the CAZymes present in a representative human mini-microbiome.

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