RESEARCH HIGHLIGHTS

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IN BRIEF

BACTERIAL GENOMICS

A time to gather chromosomes together

Bacterial secondary chromosomes replicate using mechanisms that reflect their plasmid origins. For example, the replication of chr2 in Vibrio cholerae relies on a plasmid-like origin, ori2, and a specialized regulatory factor, RctB. Importantly, unlike plasmids, the replication of secondary chromosomes occurs only once per cell cycle, which in V. cholerae is achieved by synchronizing the termination of replication with the primary chromosome (chr1). Using genetic mutants, Val et al. showed that this synchronicity is mediated by a checkpoint mechanism, in which the initiation of chr2 replication is triggered by the replication of an RctB binding site on chr1. Chromatin conformation capture data, which revealed physical contacts between chr1 and chr2, suggested that the replication machineries on the two chromosomes are then in close proximity until termination. However, the precise molecular details of the checkpoint mechanism await further characterization.

ORIGINAL ARTICLE Val, M. E. *et al*. A checkpoint control orchestrates the replication of the two chromosomes of Vibrio cholerae. Sci. Adv. **2**, e1501914 (2016)

EPIDEMIOLOGY

Which regions are vulnerable to Zika virus?

Although first discovered in 1947, Zika virus (ZIKV) had not until recently been a major public health concern. However, since its arrival in Latin America, which has been dated by genetic analysis to 2013 but was first reported in 2015, a rapid regional spread of ZIKV outbreaks has been associated with microcephaly in infants and a rare autoimmune condition of the peripheral nervous system in adults. Hay and colleagues modelled the regions that are environmentally permissive for the transmission of ZIKV. In addition to regions that have ongoing outbreaks of ZIKV, the models predicted that many other regions, such as southeastern states of the United States, parts of the Indian subcontinent, sub-Saharan Africa, southeast China and northern Australia, may be at risk. Collectively the at-risk regions are home to 2.17 billion people.

ORIGINAL ARTICLE Messina, J. P. et al. Mapping global environmental suitability for Zika virus. eLife 5, e15272 (2016)

STRUCTURAL BIOLOGY

How Cpf1 cuts its CRISPR targets

Cpf1 is a CRISPR-Cas endonuclease that, as a genome engineering tool, may have several advantages over Cas9, such as the production of staggered cuts with overhangs rather than blunt end cuts. Both Cpf1 and Cas9 use a CRISPR RNA (crRNA) to recognize target DNA, which is then cleaved using a RuvC nuclease domain. However, target cleavage by Cas9 additionally requires a HNH nuclease domain, whereas a second nuclease domain had not been identified for Cpf1. Yamano et al. and Dong et al. report crystal structures of Cpf1 that reveal a second putative nuclease domain, with a novel fold and no detectable homologues. Using mutational analysis, Yamano et al. show that this domain cleaves the target DNA at a distal site to produce the staggered cut. Remarkably, Fonfara et al. found that, in addition to DNase domains, Cpf1 has an RNase domain, which processes precursor transcripts into crRNAs. Thus, Cpf1 is an all-in-one machine for enacting CRISPR-Cas immunity.

ORIGINAL ARTICLES Yamano, T. et al. Crystal structure of Cpf1 in complex with guide RNA and target DNA. Cell <u>http://www.cell.com/cell/abstract/S0092-8674%2816%2930394-4</u> (2016) | Dong, D. et al. The crystal structure of Cpf1 in complex with CRISPR RNA. Nature <u>http://dx.doi.org/10.1038/nature17944</u> (2016) | Fonfara, I. et al. The CRISPR-associated DNA-cleaving enzyme Cpf1 also processes precursor CRISPR RNA. Nature <u>http://dx.doi.org/10.1038/nature17945</u> (2016)