Symbiotic evolution

Rhizobia are bacteria that are mutually symbiotic with leguminous plants: upon infecting their hosts, they induce the formation of nodules and fix nitrogen. The rhizobia are phylogenetically diverse and are thought to have arisen through recurrent, independent horizontal gene transfers of key symbiotic genes. However, gene transfer is not sufficient to induce symbiosis in all bacteria. Catherine Masson-Boivin and colleagues performed experimental evolution studies (*PLoS Biol.* 8, e1000280, 2010) of a nonsymbiotic bacteria, *Ralstonia solanacearum*, carrying the symbiotic plasmid of the rhizobium *Cupriavidus taiwanensis*. The authors used the resulting chimeric strain to repeatedly inoculate host plants. They recovered three clones of *Ralstonia* that were able to induce host nodulation. They then resequenced the genomes of the three experimentally evolved clones, as well as their immediate ancestors, and identified three SNPs in the *hrpG* and *hrcV* genes, which are involved in the HrpG-controlled virulence pathway. Inactivation of either gene was sufficient to confer nodulation ability on *Ralstonia*. Although nitrogen fixation was not achieved, the work shows that a recipient bacteria can rapidly evolve the ability to nodulate upon transfer of a symbiotic plasmid. ***PC***

Human methylomes

Next-generation sequencing technology applied to bisulfite-modified DNA has made possible high-resolution genomic mapping of methylcytosine. Joseph Ecker and colleagues, and Isidore Rigoutsos, Jeanne Loring and Chia-Lin Wei and colleagues, have separately reported methylomes of human embryonic stem (ES) cells and differentiated cell types (*Nature* **462**, 315–322, 2009, and *Genome Res.*, published online 4 February 2010, doi:10.1101/gr.101907.109, respectively). Their analyses identify methylcytosine in non-CG contexts and reveal widespread changes in methylation during differentiation. Ecker and colleagues found that almost 25% of methylcytosines in ES cells occur in non-CG contexts, whereas over 99% of the methylcytosines detected in fibroblasts were in the CG context. Differentiation of ES cells resulted in loss of non-CG methylation, whereas non-CG methylation was gained in fibroblast-derived induced pluripotent cells. Similarly, Rigoutsos and colleagues determined that 20% of methylcytosines in ES cells occur in non-CG contexts and that non-CG methylcytosines account for lower percentages of total methylcytosine content in three differentiated cell types. Both groups compared methylation patterns between cell types and identified differentially methylated regions, which potentially represent loci important for the regulation of differentiation-related or pluripotency-related gene expression. These methylomes are important resources for studies of mechanisms of differentiation and disease. *EN*

Chromatin regulates splicing

Recent studies have shown that exons are enriched for specific chromatin modifications, suggesting an unexpected relationship between chromatin and splicing. Tom Misteli and colleagues (*Science*, published online 4 February 2010, doi:10.1126/science.1184208) now report experimental evidence indicating that chromatin modifications influence alternative splicing. The authors examined alternative splicing events regulated by the polypyrimidine tract–binding protein PTB. They found that PTB-dependent alternatively spliced exons showed specific patterns of chromatin modifications, including differential histone H3 lysine 36 (H3K36) trimethylation. To explore a possible regulatory role for this modification, the authors altered expression of the H3K36 methyltransferase SET2 and found that such perturbations caused reciprocal changes in the splicing of PTB-dependent exons. They also found that alterations in H3K4 methylation status had similar effects on PTB-dependent alternative splicing events. The authors further examined the mechanistic basis for a subset of these regulatory events and found that, at *FGFR2*, increased H3K36 trimethylation led to recruitment of the histone tail–binding protein MRG15 and of PTB, resulting in exon exclusion. On the basis of these findings, the authors propose that differential chromatin marking recruits splicing regulators to the pre-mRNA splicing machinery, thereby influencing splicing outcome. *KV*

Treslin triggers DNA replication

In eukaryotes, DNA replication requires a strict assembly of specific proteins at the origins of replication. In vertebrates, TopBP1 is required for the initiation of DNA replication as well as for checkpoint control. William Dunphy and colleagues performed immunoprecipitation pull-down experiments in *Xenopus laevis* egg extracts to find proteins that interact with TopBP1 and identified a protein called Treslin (*Cell* **140**, 349–359, 2010). Treslin is well conserved in vertebrates and associates with replicating chromatin. The authors immunodepleted Treslin from egg extracts and found that it is required for DNA replication. Although some important events that occur before DNA replication occurred normally after immunodepletion of Treslin, the loading of Cdc45 onto replication origins was affected. The authors made antibodies to human Treslin and found that Treslin-depleted human cells have defective DNA replication and accumulate damaged DNA. The authors suggest that Treslin mediates an important step in the initiation of DNA replication in vertebrates. *PC*

Tracking pathogen evolution

Current methods to identify strains and track epidemics of hospital-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) typically involve examining a limited selection of genomic loci. Stephen Bentley and colleagues now report next-generation full-genome sequencing of MRSA strains, bringing a high level of resolution to the process of distinguishing these strains and tracking their spread and evolution on both a global and local level (*Science* 327, 469–474, 2010). The authors' first strain collection includes 43 global samples isolated from 1982 to 2003, and a second collection includes 20 samples isolated from a single hospital in Thailand over the course of 7 months. Strains were sequenced at ~23× coverage using Illumina Genome Analyzer sequencing technology. The scientists defined a core genome common to all samples and used this as a basis to reconstruct a maximum-likelihood phylogeny, which shows that strains cluster by geographic region and highlights a limited number of intercontinental transmission events. The time of the most common recent ancestor was estimated to be the 1960s, corresponding to the emergence of MRSA in Europe. The Thai samples were clustered into two groups, with five differing at only 14 SNPs, suggesting two separate introduction events and allowing direct contact tracing of transmission within this hospital setting. ***OB***

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