Transcription factor interactions

Transcription factor (TF) interactions play a key role in the development of specific tissues. Now, Yoshihide Hayashizaki and colleagues of the FANTOM Consortium map the combinatorial interactions between most DNA-binding TFs in human and in mouse (*Cell* 140, 744–752, 2010). The authors performed mammalian two-hybrid (M2H) screens to test all pairwise interactions between TFs in each organism and identified 726 and 877 TF-TF interactions in human and mouse, respectively. The authors manually assembled a list of 91 TF-TF interactions in mouse for which there was previous experimental evidence and noted that their M2H screens found 23 of these interactions. TFs with few interactions are likely to display tissue-specific expression patterns, whereas TFs that have many interactions are likely to be expressed across many tissues. Cross-species comparison of interactions showed that there were 30 conserved interactions between pairs of orthologs in the M2H data and 305 conserved interactions when literature-based evidence for interaction was also considered. The authors suggest that this transcription factor interaction atlas will enable the generation of new hypotheses on the roles of particular transcriptional networks during tissue differentiation. ***PC***

Pea aphid genome

Aphids are plant-eating insects that are model systems for insect-plant interactions as well as major pests of agricultural crops. The International Aphid Genomics Consortium now reports the draft genome sequence of the pea aphid, *Acyrthosiphon pisum* (*PLoS Biol.* **8**, e0003103, 2010). 3.3 million Sanger sequencing reads were generated, giving approximately 6.2× coverage of the estimated 517-Mb genome. 2,459 gene families displayed evidence of aphid lineage–specific duplications, more than in any other sequenced insect genome. Because the majority of aphid species are hosts to the obligate bacterial symbiont *Buchnera aphidicola*, the authors looked for evidence of lateral gene transfer between symbiont and host. Pea aphids appear to have acquired several functional genes from bacterial symbionts. Aphids undergo a series of molts before becoming adults and display polyphenism, the ability of a single genotype to develop into one of several phenotypes. Analysis of developmental genes shows that many embryonic development genes are well conserved, although many important developmental signaling pathways show aphid-specific duplications and losses. The authors suggest that such duplications may have influenced the evolution of the aphids' complex developmental trajectories. This genome sequence should be a valuable resource for investigating aphid biology as well as applied agricultural problems involving these insects. *PC*

TLR5 and metabolic syndrome

Recent studies suggest that the composition of the gut microbiota influences host metabolism and contributes to obesity. In support of this hypothesis, Andrew Gewirtz and colleagues (*Science*, published online 4 March 2010; doi:10.1126/science.1179721) show that mice lacking Toll-like receptor 5 (TLR5), a mediator of innate immunity in the gut, have hyperphagia, insulin resistance, increased adiposity and other characteristic features of human metabolic syndrome. The authors found that this phenotype was exacerbated when the mice were placed on a high-fat diet but was partially corrected when the mice were treated with broad-spectrum antibiotics to reduce the total gut bacterial load. Comparison of 16S ribosomal RNA gene sequences from the ceca of wild-type and TLR5-deficient mice revealed consistent differences in bacterial composition. To assess whether these alterations contributed to the metabolic phenotype of the knockout mice, the authors transplanted the gut microbiota from TLR5-deficient mice into wild-type germ-free mice. Notably, they found that the transplanted microbiota conferred many aspects of the metabolic phenotype to the wild-type mice, including hyperphagia, obesity and insulin resistance. These findings support the idea that variation in gut microbiota might contribute to the risk of metabolic disease in humans. *KV*

H3.3 and Atrx

H3.3 is a variant of histone H3 that is enriched in nucleosomes at transcriptionally active chromatin; the histone chaperone Hira is involved in H3.3 deposition. Now Deyou Zheng, C. David Allis and colleagues report genome-wide profiles of H3.3 localization in mouse embryonic stem cells (ESCs) and neuronal precursor cells (NPCs) (*Cell* **140**, 678–691, 2010). The authors used chromatin immunoprecipitation followed by massively parallel sequencing (ChIP-seq) to show that H3.3 is enriched in nucleosomes at active and repressed genes in ESCs and NPCs. They also profiled H3.3 localization in ESCs lacking Hira, which revealed Hira-dependent localization at active and repressed genes and Hira-independent localization at transcription factor–binding sites and telomeres. The authors used immunoaffinity purification and mass spectrometry to identify interactions between H3.3 and Atrx and Daxx proteins. H3.3 localization profiling in *Atrx*-null ESCs showed that *Atrx* is required for H3.3 localization at telomeres. Similarly, Lee Wong and colleagues recently reported that Atrx associates with H3.3 at telomeres in ESCs (*Genome Res.*, published online 28 January 2010; doi:10.1101/gr.101477.109). The multiple mechanisms of H3.3 targeting revealed here imply that H3.3 has distinct functions at different genomic regions. *EN*

Melanoma transcriptome

Levi Garraway and colleagues report an integrative genomic analysis of the melanoma transcriptome based on high-throughput paired-end sequencing of cDNA (RNA-seq) of ten cell lines or short-term cultures derived from patients with metastatic melanoma (*Genome Res.*, published online 23 February 2010; doi/10.1101/gr.103697.109). Their dataset reliably covers approximately 12% of protein-coding genes. They identified 11 novel gene fusions resulting from chromosomal rearrangements. They used Affymetrix 6.0 SNP arrays on genomic DNA taken from the same samples to measure copy number changes, and Sanger sequencing to map the breakpoints to base-pair resolution. The fusion transcripts were found to be individually rare, with none observed in more than one sample or found in an additional 90 melanoma cell lines or short-term cultures from patients. The authors also identified 12 novel read-through chimeric transcripts, including a recurrent transcript involving *CDK2*. They further used the RNA-seq dataset to characterize sequence mutations, gene expression, alternative splicing and allele-specific expression. They estimated a somatic mutation rate approximately 4–8× higher than that commonly found in other cancers, indicating an elevated mutation rate during melanoma progression, which is thought to be correlated with UV exposure. ***OB***

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