Plastic tunicate genome

The larvacean tunicate *Oikopleura dioica* lives in the open sea and displays chordate morphology. Daniel Chourrout, Patrick Wincker and colleagues now report sequencing of its 70 Mb genome (*Science* 330, 1381–1385, 2010). Compared to other metazoans, *Oikopleura* shows fast rates of protein evolution, which may be related to the absence of DNA repair proteins in its genome and the mutagenic environment of the ocean surface. Approximately 18,000 genes are predicted in the compact *Oikopleura* genome. Introns and intergenic regions are small, and transposable elements are relatively infrequent. Interestingly, a subset of genes enriched for developmental transcription factors display longer introns and intergenic regions, suggesting that compaction is harmful in this genomic context. Analysis of 5,589 introns showed that 76% had positions unique to *Oikopleura* compared to other species. The authors provide some evidence that reverse splicing, the mechanism by which introns that have been spliced out are ectopically reinserted into transcripts, may have contributed to this large percentage of recently gained introns. Low levels of chromosomal synteny were seen between *Oikopleura* and other invertebrates, and local gene order in *Oikopleura* is indistinguishable from random gene order. The authors suggest that conservation of genome architecture is not required for the conservation of ancestral morphologies. ***PC***

Sirt6, growth and obesity

In yeast, *SIR2* is required for lifespan extension caused by caloric restriction. The sirtuin family of proteins has also been associated with metabolic regulation and stress tolerance, although it is not clear whether sirtuins act as longevity factors in mammals. Frederick Alt and colleagues now report that mice that specifically lack *Sirt6* in the brain ($BS6^{ko}$) display postnatal growth retardation and obesity (*Proc. Natl. Acad. Sci. USA*, published online, doi:10.1073/pnas.1016306107, 22 November 2010). $BS6^{ko}$ mice were significantly smaller than wildtype littermates at 4 weeks of age, although by 6–7 weeks of age, they were not distinguishable from wildtype mice. Pituitaries from $BS6^{ko}$ mice appeared to have a growth hormone (GH) deficiency despite normal levels of growth hormone–releasing hormone (GHRH) and somatotropin release–inhibiting hormone (SRIH) transcript levels. $BS6^{ko}$ mice displayed increased adiposity by 6–8 months of age, likely through lower levels of GH and hypothalamic neuropeptides. Sirt6 is known to deacetylate the two chromatin marks H3K9 and H3K56. $BS6^{ko}$ mice display H3K9 hyperacetylation in the hippocampus and hypothalamus and H3K57 hyperacetylation in the hypothalamus, cortex, hippocampus and cerebellum. This study shows a role for *Sirt6* in somatic growth and adult-onset obesity in mouse. *PC*

GNA11 and uveal melanoma

Previous work showed that activating mutations in codon 209 of the G-protein alpha subunit gene *GNAQ* occur in more than 40% of uveal melanomas. Boris Bastian and colleagues now report (*N. Engl. J. Med.* **363**, 2191–2199, 2010) that activating mutations in a related gene, *GNA11*, also occur at high frequency in uveal melanomas. The authors examined 713 melanocytic neoplasms, including 139 blue nevi, 163 primary uveal melanomas and 23 metastatic uveal melanomas, for mutations in *GNAQ* and *GNA11*. Consistent with earlier work, they found mutations in codon 209 of *GNAQ* in 55% of blue nevi, 45% of primary uveal melanomas and 22% of metastatic uveal melanomas. Mutations affecting codon 209 of *GNA11* showed an opposite trend in frequency, occurring in 6% of blue nevi, 32% of primary uveal melanomas and 56% of metastatic uveal melanomas. Mutations in codon 183 of *GNAQ* or *GNA11* were also found in a subset of tumors (<5%). Notably, melanocytes transduced with the *GNA11* Gln209Leu or Arg183Cys variants formed rapidly growing tumors when injected into mice, with the Gln209Leu variant producing a high frequency of metastases. The transduced melanocytes also showed activation of the MAP kinase pathway, suggesting that tumors with these mutations might be sensitive to MEK inhibitors. *KV*

Cold air triggers COLDAIR

Vernalization is the process by which plants acquire the ability to flower rapidly following exposure to prolonged cold temperatures. In *Arabidopsis*, this process involves stable silencing of the floral repressor *FLC* by polycomb repressive complex 2 (PRC2). Now, Sibum Sung and Jae Bok Heo identify a noncoding RNA called COLDAIR that is required for polycomb-mediated repression of *FLC* (*Science*, published online, doi://10.1126/science.1197349, 2 December 2010). The authors showed that COLDAIR is transcribed from an intron within *FLC* and expression of COLDAIR transiently increases during vernalizing cold exposure. The authors used RNAi to knockdown COLDAIR, which caused delayed flowering after vernalization. This phenotype is consistent with the higher level of FLC expression in COLDAIR knockdowns. COLDAIR-mediated repression of *FLC* is specific, as other related floral repressors are not affected by COLDAIR knockdown. The authors used RNA binding assays to show that COLDAIR RNA directly interacts with the CLF protein, a component of PRC2, and this association is increased during cold exposure. Using chromatin immunoprecipitation, the authors showed that COLDAIR knockdown results in decreased CLF occupancy at the *FLC* locus and decreased levels of the repressive histone modification H3K27me3 at the *FLC* locus. *EN*

FOXO, muscle and aging

Forkhead box O (FOXO) transcription factors have been implicated in the regulation of aging in many organisms; for example, FOXO overexpression in the *Drosophila* fat body extends life span. Now, Fabio Demontis and Norbert Perrimon report that *FOXO* expression in *Drosophila* muscle regulates aging processes (*Cell* 142, 813–825, 2010). The authors first identified protein aggregates that accumulate in the muscles of old flies and showed that muscle-specific FOXO overexpression delays accumulation of these aggregates. Similarly, overexpression of 4E-BP, a target of FOXO, decreases aggregate formation. Flies overexpressing FOXO or 4E-BP in muscle retain muscle strength during aging, as measured by climbing and flying tests, and have extended longevity. These flies displayed reduced food intake, suggesting overlapping mechanisms with lifespan extension by calorie restriction. Interestingly, FOXO overexpression in muscle decreased accumulation of protein aggregates in retina, brain and adipose tissues as well, indicating that aging processes in muscle effect aging processes in other tissues. The authors show a prolonged presence of autophagosomes in FOXO-overexpressing muscle and that knockdown of a key autophagy gene partially counteracts the effect of FOXO overexpression on protein aggregation, suggesting that FOXO functions to delay aging in part by promoting autophagic functions. ***EN***

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