Oxytricha macronuclear genome

All ciliates have both a micronucleus, which is mostly inactive during vegetative growth, and a macronucleus, which is enlarged (owing to DNA amplification) and transcriptionally active. In *Oxytricha trifallax*, 96% of the micronuclear genome is eliminated during formation of the macronucleus. The macronuclear genome in *Oxytricha* is composed of tens of thousands of tiny chromosomes. Laura Landweber and colleagues now report the first *Oxytricha* macronuclear genome (*PLoS Biol.* 11, e1001473, 2013). The authors found very high levels of nucleotide diversity, with mean SNP heterozygosity of 4.0%. The authors estimated that the haploid number of nanochromosomes was ~15,600, with a mean length of ~3.2 kb. Extensive alternative fragmentation, in which there are multiple versions of nanochromosomes that have overlapping genic regions, was observed in up to 40% of surveyed nanochromosomes. Nanochromosome copy number was also highly variable, as was nanochromosome length. The authors note that the most remarkable aspect of this macronuclear genome is the number of telomeres, which are present on every nanochromosome. Not surprisingly, this organism has acquired multiple new telomere-binding proteins. ***PF***

PKCζ is a metabolic tumor suppressor

Cancer cells require high amounts of energy to maintain rapid growth and proliferation and exhibit adaptive plasticity in their metabolism to meet these energy needs. Now, Jorge Moscat and colleagues show that loss of protein kinase Cζ (PKCζ) promotes the metabolic plasticity that cancer cells require (*Cell* **152**, 599–611, 2013). The authors first knocked down PKCζ in SW480 cells and cultured these without medium changes, leading to nutrient exhaustion. Whereas control cells decreased in number, the proliferation of cells lacking PKCζ was not affected. Transcriptome analysis suggested that PKCζ-deficient cells used glutamine instead of glucose. Further experiments showed that serine-glycine biosynthesis was increased in cells using glutamine and that one of the functions of PKCζ is to redirect metabolism to a more efficient use of glutamine. To explore the metabolic effects of PKCζ loss *in vivo*, the authors implanted PKCζ-deficient cells in nude mice. They found that the growth rate of PKCζ-deficient xenografts was higher than that of controls. Analysis of several gene expression data sets from human colorectal tumors showed a loss of PKCζ expression. The authors conclude that PKCζ has an important role in metabolic plasticity in cancer cells, and potential treatments that counteract the well-known Warburg effect may be effective if PKCζ is activated. *PF*

Pigeon genome

Michael Shapiro and colleagues report the reference genome for the domestic rock pigeon, *Columba livia* (*Science*, published online 31 January 2013; doi:10.1126/science.1230422). The authors sequenced the whole genome of a male Danish tumbler pigeon to over 60-fold coverage using the Illumina HiSeq 2000 platform and carried out *de novo* assembly. They also resequenced 40 additional rock pigeon genomes, representing 36 domestic breeds and 2 feral pigeons, with 8- to 26-fold coverage each. They report estimates of genetic diversity and mutation rate that are comparable to those found in other avian species, as well as a large and stable effective population size. Their annotation identified 17,300 genes, with most of these also found in other avian genomes. Phylogenetic analysis was used to define the origins of rock pigeon breeds and their relationships with the hill pigeon, *Columba rupestris*. The authors also identified a common variant in *EphB2* associated with the head crest phenotype, in the resequenced panel, as well as in an additional 61 crested and 69 uncrested birds. They suggest a mechanism by which *EphB2* may influence feather polarity during development and demonstrate that the pigeon is a useful model to characterize derived traits in domesticated birds. *OB*

Recurrent mutations in meningiomas

Meningiomas, the most common primary brain tumors, frequently harbor somatic mutations in the tumor suppressor gene *NF2*. To gain further insights into the etiology of these tumors, Murat Günel and colleagues performed exome sequencing of 50 meningiomas followed by targeted resequencing of selected genes in 250 additional meningiomas (*Science*, published online 24 January 2013; doi:10.1126/science.1233009). They found *NF2* mutations in 36% of tumors and also identified recurrent mutations in *TRAF7*, *KLF4*, *AKT1* and *SMO*. *TRAF7* mutations were detected in 24% of tumors and frequently co-occurred with *KLF4* mutations. Conversely, *TRAF7* and *KLF4* mutations were never observed in tumors with *NF2* mutations. The authors also identified a recurrent activating mutation of *AKT1* in 13% of tumors, as well as likely activating mutations of the Hedgehog pathway effector gene *SMO* in 4% of tumors. In an independent sequencing study of meningiomas, Rameen Beroukhim and colleagues report the discovery of similar activating *AKT1* and *SMO* mutations, as well as recurrent mutations in chromatin-modifier genes (*Nat. Genet.* **45**, 285–289, 2013). Together, these studies identify a subset of patients with meningiomas that could benefit from targeted therapies aimed at inhibiting the AKT and Hedgehog signaling pathways. *KV*

TET function in primordial germ cells

Developmentally programmed global loss of 5-methylcytosine (5mC) involves the TET1 and TET2 enzymes that convert 5mC to 5-hydroxymethylcytosine (5hmC). TET enzyme function has been investigated in embryonic stem cells, and Azim Surani and colleagues now report a functional investigation of 5hmC in mouse primordial germ cells (PGCs) (*Science* 339, 448–452, 2013). The authors isolated PGCs and profiled genomic patterns of 5mC and 5hmC. They showed that Tet1 and Tet2 are expressed in PGCs at the time of loss of 5mC and gain of 5hmC and that 5mC erasure is coupled to 5hmC enrichment. They found that, after the peak of 5hmC conversion, the levels of 5hmC were progressively depleted, indicating a process of replication-coupled dilution. The authors created an inducible system for the double knockdown of *Tet1* and *Tet2* in cultured PGC-like cells; this resulted in inhibition of 5mC demethylation. Conversely, overexpression of Tet1 and Tet2 promoted 5mC erasure. Whole-genome bisulfite sequencing showed that a number of loci, mostly repeat elements, escape demethylation. This work establishes a role for TET enzymes and 5hmC in the process of DNA demethylation in developing primordial germ cells. ***EN***

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