Ebola genomes track virus evolution in real-time epidemic

Pardis Sabeti and colleagues report the whole-genome sequencing of 99 Ebola virus samples from 78 patients in Sierra Leone collected during the course of the epidemic there this year (*Science* doi:10.1126/science.1259657; 28 August 2014). They also include comparisons to 20 Ebola virus genomes from earlier outbreaks, including three from Guinean samples. The current outbreak started in Guinea in West Africa in February 2014 and spread to Liberia, Sierra Leone and Nigeria. This work suggests direct patient-to-patient transmission from Guinea to Sierra Leone, coinciding with the first confirmed case of Ebola virus disease in Sierra Leone in late May. They further identify two distinct viral lineages in the first 12 Sierra Leone patients, who may have been infected during a funeral that they all attended. The availability of multiple samples for some patients allowed the identification of variations within a single host. By monitoring the single-nucleotide variants (SNVs) that later became fixed in other patients and increased in frequency in the population, the authors were able to systematically track the emergence of a third viral lineage. Their work suggests that the current epidemics may be explained by human-to-human transmission, following on a zoonotic transmission event from Central Africa that occurred in the past decade. *OB*

Chromatin looping and globin expression

Engineered expression of fetal forms of hemoglobin has potential therapeutic use in treating individuals with hemoglobinopathies, for whom elevated expression of fetal globin in adulthood is beneficial. Now, Gerd Blobel and colleagues report that fetal globin expression can be reactivated in mouse and human adult erythroblasts through forced chromatin looping by an engineered zinc-finger (ZF) protein (*Cell* **158**, 849–860, 2014). The authors created a custom ZF protein that binds to mouse embryonic globin promoter sequences. They fused the ZF to the self-association domain (SA) of Ldb1, a transcription factor involved in the formation of loops between globin gene promoters and the locus control region (LCR), a distal enhancer that drives developmental expression of the globin genes. Expression of the ZF-SA protein in primary adult erythroblasts increased embryonic globin expression by almost 800-fold. The authors also used another engineered ZF-SA protein that binds to human fetal globin gene promoters and showed that it induces chromatin looping between the fetal globin gene promoter and the LCR and activates fetal globin expression in primary adult human erythroid cells. *EN*

Mutational landscape of chromophobe renal cell carcinoma

W. Kimryn Rathmell, Chad Creighton and colleagues report the genomic analysis of 66 chromophobe renal cell carcinomas (ChRCCs), which constitute a rare subtype of kidney cancer, and matched normal tissue (*Cancer Cell* **26**, 319–330, 2014). The researchers analyzed whole-exome sequence, gene expression profiles and CpG methylation profiles from all 66 tumor-normal pairs, whole-genome sequence from 50 pairs and mitochondrial DNA sequence form 61 pairs. The driver genes *TP53* and/or *PTEN* were found to be significantly mutated in 53% of the samples. Six of the 50 whole genome–sequenced tumors also showed rearrangements involving the *TERT* promoter, which led to higher levels of *TERT* expression. Finally, by comparison to available data on clear cell renal cell carcinoma (ccRCC), the authors found that ChRCC and ccRCC have distinct anatomical origins, as reflected in their diverged patterns of gene expression and methylation. ChRCC had increased expression of genes encoding enzymes of the Krebs cycle, whose expression is strongly suppressed in ccRCC. The results indicate that these two related tumor types support tumor growth through different bioenergetics strategies. *BL*

Written by Orli Bahcall, Brooke LaFlamme, Emily Niemitz & Kyle Vogan

Single-cell genomics in the brain

Christopher Walsh and colleagues report the identification of large somatic copy number variants (CNVs) in the human brain by single-cell whole-genome sequencing (*Cell Rep.* doi:10.1016/j.celrep.2014.07.043; 21 August 2014). The authors isolated over 200 neuronal and non-neuronal cells from the post-mortem brains of three normal adults, one fetus with trisomy 18 and one adult with hemimegalencephaly (HMG). These sequences were also compared to the genomes of 24 single cultured lymphoblast cells. Cells from the fetal brain all showed an estimated three copies of chromosome 18, as expected, whereas over 95% of cells from normal brains had no detectable aneuploidy. However, the existence of a small proportion of cells with large CNVs suggests that somatic CNVs may arise normally during development. Although only eight cells from the HMG brain yielded sequences of sufficient quality for analysis, the authors were able to show that only one of the eight cells had a copy number gain at 1q, confirming previous results of mosaic gain of 1q and providing an estimate of its prevalence in diseased brain. The findings highlight the usefulness of single-cell whole-genome sequencing. They also indicate that CNVs in even a minority of brain cells can have large phenotypic effects. *BL*

Hummingbird taste perception

The ability of hummingbirds to detect sugar-rich nectar allows them to occupy a distinct ecological niche, but the basis for this adaptation was unknown. Maude Baldwin, Stephen Liberles and colleagues (*Science* **345**, 929–933, 2014) have now used comparative genomics and functional studies to determine how hummingbirds perceive sweet taste. In most vertebrates, the ability to detect savory and sweet tastes is mediated by specialized G protein–coupled receptors (T1Rs), with T1R1-T1R3 heterodimers responding to savory compounds and T1R2-T1R3 heterodimers responding to sweet compounds. The authors analyzed the T1R gene repertoire of hummingbirds in comparison to other vertebrates and found that hummingbirds, like other bird species, lack genes encoding T1R2 receptors. They then performed functional studies and found that hummingbird T1R1-T1R3 heterodimers, unlike chicken or swift T1R1-T1R3 heterodimers, could respond to several sugars. They further analyzed T1R3 protein chimeras and identified a 19-amino-acid segment in hummingbird T1R3 that was sufficient to confer sensitivity to sucrose. Similarly, they also found evidence that hummingbird T1R1 has undergone adaptive changes contributing to the perception of sweet taste. Together, these findings indicate that hummingbirds have acquired adaptive changes in T1R1 and T1R3 that have altered their ligand specificity to allow the detection of sugars. *KV*