EBOLA

Sequencing on the ground

The West African Ebola epidemic that began in 2014, and still threatens to re-emerge, prompted a flurry of efforts to sequence the genome of the virus as it spread. Genomic information can contribute to epidemiological tracking, identify mutations that increase the disease's virulence and inform therapeutic strategies. But sequences must be obtained fast if they are to help to control a raging epidemic.

On page 228 of this issue, Quick *et al.* describe a portable, real-time sequencing system that they used in local, resource-poor sites in Guinea during 2015 (J. Quick *et al. Nature* **530,** 228–232; 2016). The requisite equipment, including the tiny MinION genome sequencer (pictured), fitted into 50 kilograms of standard airline luggage. The researchers generated sequence data within 24 hours of receiving a patient's viral RNA sample — days to weeks less than it would have taken to receive data from a central sequencing facility. **Marian Turner**

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GENETICS

Asymmetric breaks in DNA cause sterility

The part that the mouse gene *Prdm9* plays in generating double-strand breaks in DNA has now been linked to its putative role in speciation, thanks to experiments that use a 'humanized' version of the gene. **SEE ARTICLE P.171**

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During the specialized meiotic cell divisions that produce mammalian eggs and sperm, an individual's two sets of chromosomes are shuffled in a process called meiotic recombination, producing genetically unique chromosomes to pass on to offspring. Recombination tends to occur in DNA regions known as hotspots, the locations of which are determined by a single DNA-binding protein, PRDM9. The presence of different versions (alleles) of the *Prdm9* gene in two subspecies of mice renders the hybrid offspring of these subspecies sterile[1], but how the gene exerts this effect has been unknown. On page 171 of this issue, Davies *et al.*[2] link these two roles of *Prdm9*. They find that it is the rapid subspecies-specific degradation of *Prdm9* DNA-binding sites that underlies sterility in mouse hybrids.

The male offspring of crosses between the mouse subspecies *Mus musculus musculus* and *Mus musculus domesticus* are sterile. It has been proposed that sterility arises for two reasons. First, the chromosomes from the two subspecies do not recognize one another normally because their DNA sequences have diverged, so they do not align correctly — to use the technical terminology, they do not synapse. Such asynapsis results in the death of sperm-cell progenitors, although the mechanism underlying this process is not well understood. Second, transcription from the sex chromosomes is not inhibited as it is in the meiosis of healthy testes[3].

Both of these defects can prevent normal sperm development. The extent of the damage is regulated by interaction between the different alleles of *Prdm9* and another gene, *Hstx2*, that are present in each subspecies[1,4]. But an understanding of which diverging sequences prevent synapsis, and of the molecular mechanisms underlying the roles of *Prdm9* and *Hstx2*, has remained out of reach.

Davies *et al.* now report considerable progress in defining the role of *Prdm9* in hybrid sterility. They focused on a structure called the Cys_2His_2 zinc-finger domain of mouse PRDM9, which is responsible fo r the protein's ability to bind to specific DNA sequences. DNA binding enables PRDM9 to add methyl groups to a lysine amino-acid residue on the protein histone H3, around which DNA is packaged in the nucleus. Such methylation is a prerequisite for the production of double-strand breaks (DSBs) in nearby DNA; these breaks are subsequently repaired through meiotic recombination, with the unbroken equivalent chromosome (the homologous chromosome) used as a genetic template for repair[5].

The authors engineered a 'humanized' form of *Prdm9*, in which they replaced the zinc-finger domain from *M. m. domesticus Prdm9* with the equivalent sequence from the human gene, which binds to a different DNA sequence. The humanized male mice were fertile but displayed a pattern of recombination hotspots that shared little overlap with the hotspots of wild-type *M. m. domesticus* mice. Davies and colleagues then crossed the humanized males to