Nature Reviews Genetics | AOP, published online 11 November 2014

IN BRIEF

MODEL ORGANISMS

Host determinants of Ebola virus pathogenicity

Laboratory studies of Ebola virus infection have suffered from a lack of mouse models that recapitulate some of the pathology seen in humans, such as Ebola haemorrhagic fever (EHF). Using genetically diverse mouse strains from the Collaborative Cross project, Rasmussen and Okumura *et al.* found a range of susceptibilities to Ebola virus, from resistant mouse strains to those that were susceptible and showed many of the known human pathologies. The authors also identified host genetic and transcriptional signatures that correlate with infection severity. This study paves the way for further detailed mouse studies of Ebola virus infection and may inform both the genetic determinants of Ebola virus susceptibility in humans and possible therapeutic approaches to limit pathogenesis.

ORIGINAL RESEARCH PAPER Rasmussen, A. L. & Okumura, A. *et al.* Host genetic diversity enables Ebola hemorrhagic fever pathogenesis and resistance. *Science* http://dx.doi.org/10.1126/science.1259595 (2014)

CHROMOSOME BIOLOGY

A high-quality mouse Y chromosome sequence

The male-specific region of the Y chromosome (MSY) in mice has been difficult to sequence because its repetitive nature and resistance to recombination preclude the accurate mapping of sequence reads. Soh *et al.* developed the single-haplotype iterative mapping and sequencing (SHIMS) method and report a reference MSY sequence to ~99% completion. Although the placental mammals have a shared evolutionary origin of Y chromosomes, the mouse MSY is strikingly different from its primate counterparts: its intrachromosomal amplification of testis-expressed genes is far more extensive, meaning that it has a highly genic and euchromatic make-up, in contrast to the largely heterochromatic human Y chromosome.

ORIGINAL RESEARCH PAPER Soh, Y. Q. S. *et al.* Sequencing the mouse Y chromosome reveals convergent gene acquisition and amplification on both sex chromosomes. *Cell* http://dx.doi.org/10.1016/j.cell.2014.09.052 (2014)

DISEASE GENETICS

New insights into the genetic architecture of ASDs

De novo mutations are spontaneous mutations that are detected in a child but not in either parent. Two well-powered family-based exome sequencing studies targeting *de novo* mutations reveal novel insights into the genetic architecture of autism spectrum disorders (ASDs). The first study by Iossifov *et al.* analysed the genomes of >2,500 'simplex' families — that is, families in which neither parent nor siblings of a child with ASD are affected — and showed that 13% of *de novo* missense mutations and 43% of *de novo* likely gene-disrupting mutations contribute to 12% and 9% of diagnoses, respectively. Of note, genes affected by spontaneous mutations were often expressed during embryonic development or encoded chromatin-remodelling proteins. The latter finding was also reported in the second study by De Rubeis *et al.*, who sequenced the exomes of 3,871 autism cases and 9,937 ancestry-matched or parental controls. The researchers also found that mutated genes were enriched for those encoding products involved in synaptic formation and transcriptional regulation. Together, these studies highlight the promising role of exome sequencing for the discovery of disease-relevant genes in neuropsychiatric disease.

ORIGINAL RESEARCH PAPERS Iossifov, I. *et al.* The contribution of *de novo* coding mutations to autism spectrum disorder. *Nature* http://dx.doi.org/10.1038/nature13908 (2014) | De Rubeis, S. *et al.* Synaptic, transcriptional and chromatin genes disrupted in autism. *Nature* http://dx.doi.org/10.1038/nature13772 (2014)