IN THE NEWS

No Mickey Mouse science

"For hundreds of years we have watched curiously as mice run round wheels, press levers or navigate mazes. Finally we have the genetic blueprint that will unveil the mysteries of the mouse" (*The Times*). This is how Simon Festing of the Association of Medical Charities described the achievement published in the 5 December issue of *Nature*. "The mouse sequence is the phrasebook that is transforming our ability to translate the human book of life." (*The Financial Times*) said Jane Rodgers of the Sanger Centre.

"Scientists have attached such an importance to the murine genome that its [draft] sequence has been completed three years after the project was launched" (*The Times*) and the finished sequence is expected in 2005. The international consortium used the shotgun method, previously used by Celera to sequence the human and mouse genomes (both of which have been available to subscribers for 18 months). Craig Venter, the former director of Celera, said he felt "wonderfully vindicated that they [the consortium] have seen the power of a whole genome shotgun" (*The New York Times*).

"Even the genomes for small creatures are huge", says *The Guardian*, for the mouse genome is 2.9 billion bp long. Its analysis revealed that mice and humans "share the same genes for blood pressure, temperature regulation, bone manufacture, cell division, tissue growth and so on." (*The Guardian*) The sequence is complicated — "it's rather like being dropped into the middle of Tokyo with no knowledge of Japanese, and being asked to find your way around using a local newspaper" says Ewan Birney (*The Times*), so his task will be to develop "a guidebook or phrasebook, something that tells us what's good, what's bad and what's boring about this genome" (*The Times*).

Magdalena Skipper

MOUSE GENOME

The mighty mouse

The strains of mice that are widely used in laboratories today originated mainly from mouse fanciers who bred hybrids of *Mus mus musculus* and *M. m. domesticus*, and who have inbred the mouse lines extensively to create ~50 commonly used strains. Now, the mighty mouse has come to the rescue again with its ultimate contribution: the sequences of both its genome and its transcriptome, published in the December 5 issue of *Nature*. Through analysis of the initial sequences, we will learn much more about mammalian life, and about ourselves.

The 2.5-Gb mouse genome sequence, from the C57BL/6J strain, covers 96% of the euchromatic sequence. According to the Mouse Genome Sequencing Consortium, 99% of mouse genes are directly homologous to human genes, even though the mouse genome is 14% smaller than the human one. This further strengthens the idea that mammalian life can be built on only ~30,000 genes, as novel gene-prediction programs developed for this work suggest that the mouse too has approximately that number.

To understand further the mouse transcriptome, an international consortium sequenced more than 1.4 million expressed sequences, from which they described 37,806 individual 'transcriptional units'. In a boost to research, each of the sequences reported in the transcriptome paper is backed up by a freely available physical clone, generating a valuable resource for the community. As ~4,000 of these transcripts are probably not translated, this too suggests that both mice and humans are built from at least 30,000 genes, although the presence of additional end sequences suggests there might be more genes not represented in the consortium's clone collection at present. So, we seem to have about the same number of genes, 99% of these genes have similar sequence, and we both like cheese. Then why aren't mice more like us? The answer probably lies in the regulation of

MOUSE GENOME

A high-resolution atlas

Down syndrome is the most common cause of mental retardation in humans. Through a yet unknown mechanism, the presence of an extra copy of human chromosome 21 (HSA21) causes developmental defects in many organs, most notably the brain. HSA21 was the second human chromosome to be fully mapped and sequenced, and now two groups report the first comprehensive analysis of the expression patterns of HSA21 genes in the mouse. These 'atlases' promise to be a valuable resource for identifying the genes that underlie Down syndrome.

The two groups — Reymond *et al*. and The HSA21 Expression Map Initiative — identified the mouse orthologues of the 213 genes on HSA21, of which 178 are confirmed, and isolated cDNA fragments corresponding to these genes. Then, using complementary approaches, they looked at their expression in different tissues and at different developmental stages of mouse embryogenesis using reverse transcriptase PCR and mRNA *in situ* hybridization. In addition to this 'wet bench' approach, The HSA21 Expression Map Initiative relied heavily on informatics to measure their frequency in publicly available mouse EST libraries and to identify genes with similar expression profiles. They also conducted mRNA *in situ* hybridization, focusing on whole embryos and on the neonatal brain. Both groups have deposited their data in a web interactive database.

Together, these studies highlighted several HSA21 genes that, because of their expression in the tissues and organs that are most severely affected by Down syndrome, are good candidates for further investigation. Interestingly, the expression of many HSA21 genes is ubiquitous in early embryogenesis, but becomes more restricted as development proceeds. This is consistent with findings by The HSA21 Expression Map Initiative, who showed that genes found exclusively in multicellular organisms are more likely to be expressed in a spatially or time-restricted pattern, compared with the ubiquitous expression of those genes that are also found in yeast. Both groups also observed genes with similar expression patterns that cluster on particular