100 YEARS AGO

While walking along the main road on the outskirts of Bordighera yesterday morning, I noticed a strange-looking insect moving across it in a peculiar way. On getting nearer, I saw that what had attracted my notice was a black ant — about an inch long with brown wings — dragging a cricket bigger than itself… A low wall ran alongside the road, and when the ant got within six feet of it a common brown lizard appeared on the top of the wall and evidently soon caught sight of the ant, for it ran quickly down the wall and to within two feet of it, when it crouched for a second or two like a cat ready to spring, and then charged the ant, apparently butting the cricket free with its head. Before the ant could regain its hold the lizard seized the cricket in its mouth, and darted up the wall in the direction from which it originally appeared on the scene, leaving the ant running round and round, moving its wings in an agitated manner, vainly searching for its lost prey.

From *Nature* 22 October 1903.

50 YEARS AGO

Montegazza observed the survival of human spermatozoa after exposure to a temperature of –15 °C. He speculated that in the future, frozen semen might be used in animal husbandry and even proposed that a man dying on the battlefield might, by his wife, beget a legitimate child after his own death… Work in our laboratory, recently, indicated that treatment with 10 per cent glycerol prior to freezing with 'dry ice' produced an average 67 per cent survival of human spermatozoa obtained from five young healthy men… Three recipients have been successfully inseminated with frozen semen: one woman, nulliparous, has missed six menstrual periods, has cervical softening and uterine enlargement, and has developed other signs of pregnancy. The second woman, primiparous, has subjective signs of pregnancy, and one week after her first missed menses the Aschheim–Zondek test was suggestive; following an additional seven days of observation the test became positive. Five menses have not occurred. An X-ray film shows a normal developing foetal skeleton. The third recipient, nulliparous, has missed three menses and the Aschheim–Zondek test is positive.

From *Nature* 24 October 1953.

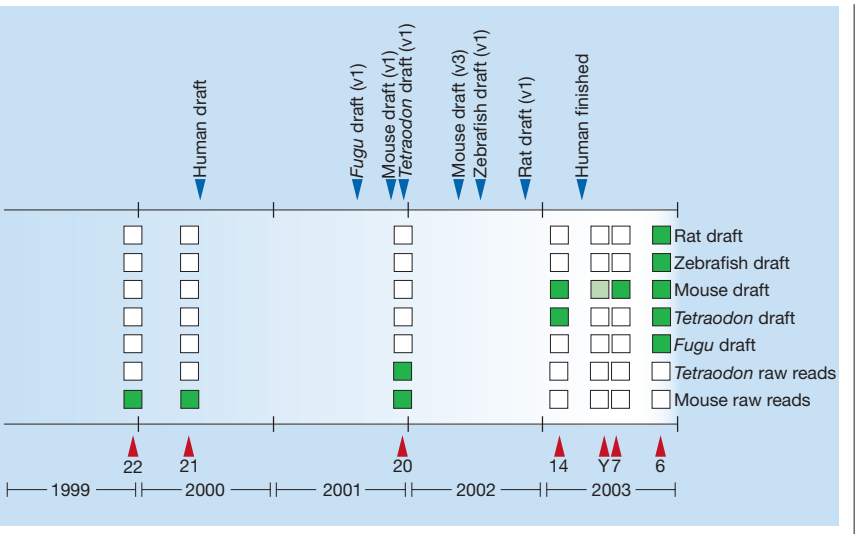

Figure 2 **Comparative benefits. The increasing availability of draft genome sequences for other vertebrates is allowing better predictions of which stretches of human DNA constitute genes. This timeline shows the publication dates of the finished human chromosomes 22, 21, 20, 14, Y, 7 and 6. The green boxes indicate the cross-species comparisons that were included in the papers concerned; *Fugu* and *Tetraodon* are species of pufferfish that were chosen for sequencing because of their compact genomes. Sequencing proceeds from 'raw reads', to drafts of various versions, to finished; the light green box indicates the — obviously — limited comparison possible of the human Y chromosome with the draft sequence of a female mouse.**

techniques have proved ineffective in teasing them apart.

However, full analyses of the remaining 17 chromosomes should be well worth the wait. As their description of chromosome 6 shows, Mungall *et al.*[1] have been the first to be able to fully apply the cross-species comparative power that is now on offer as the DNA sequences of other organisms become available (Fig. 2). Assembled draft genomes of the mouse, rat, *Tetraodon* (spotted green pufferfish), *Fugu* (tiger pufferfish) and zebrafish are in hand, and can now be used to search for regions of similarity or conservation between different organisms. This comparative approach allows refined predictions of which stretches of DNA are actually genes, and a more sophisticated interpretation of the underlying genomic data. The power of comparative genomics will grow as the genome sequences of the chicken, chimpanzee, frog, dog and cow, already in the production queue, become available.

Several other large-scale projects also have the aim of understanding how life functions at the biomolecular level. The newest of them, ENCODE (for 'Encyclopedia of DNA Elements')[7], involves a microscopic examination of 30 million bases of the human genome (about 1%). The aim is to identify all of the functional elements and to create a type of *Peterson Field Guide* to DNA. This electronic book will contain descriptions, examples and identifying characteristics of each type of known DNA component; these can then be used to scan the rest of the genome and other genomes for similar pieces of DNA sequence that might have a similar function. The ENCODE project encompasses both protein-coding elements and non-coding functional elements that do not themselves code for protein but instead regulate the production or expression of proteins from nearby genes.

Another project, MGC (the 'Mammalian Gene Collection')[8], is attempting to amass at least one full-length messenger RNA transcript for each gene in the human and mouse genomes. Zebrafish and frog mRNAs are also now being included in this collection. These transcript sequences are vital for the continuing annotation of the human genome, in that they provide a complete picture of the entire gene after it has been spliced from the genome. Moreover, the mRNA clones can be introduced into a foreign host cell and made to produce a specific protein. These proteins can then be tested for functional activity. Similar projects are continuing worldwide, providing resources from a variety of organisms. All will help in interpreting the mysteries still buried in the DNA sequence of the human genome. ■

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