50 Years Ago

'Extracorporeal perfusion of the isolated head of a dog' — Critical evaluation of cerebral metabolism and intracranial fluid distribution necessitates complete isolation of the brain's blood supply; however, brain viability must be demonstrated and maintained for such studies to be meaningful … In order to minimize handling of the brain substance, a factor which may disturb fluid distribution and cerebral metabolism, we have chosen to leave the brain within the skull during perfusion … Most cortical activity ceased when blood glucose was depleted … Even after the electrocortical activity ceased, corneal and lid reflexes remained intact and the oxygen and glucose consumption continued … From our experience, we believe that electrocortical activity is a sensitive index of brain viability, in that it is lost long before inactivation of corneal and lid reflexes or cessation of metabolism. In this preparation we have demonstrated that the dog brain maintains this activity for several hours after complete decapitation.
From *Nature* 25 April 1964

100 Years Ago

The second reading of a Bill to prohibit experiments on dogs was carried in the House of Commons on Friday last, April 17, by a majority of forty-two … It was stated on behalf of the Government that an amendment will be moved in Committee to abolish the proposed prohibition and to allow experiments only in cases where no other animal but a dog is available for the purpose … Before the second reading was taken, a memorial signed by more than three hundred eminent physicians, surgeons, and other scientific investigators, protesting against the measure, was addressed to the Home Secretary.
From *Nature* 23 April 1914

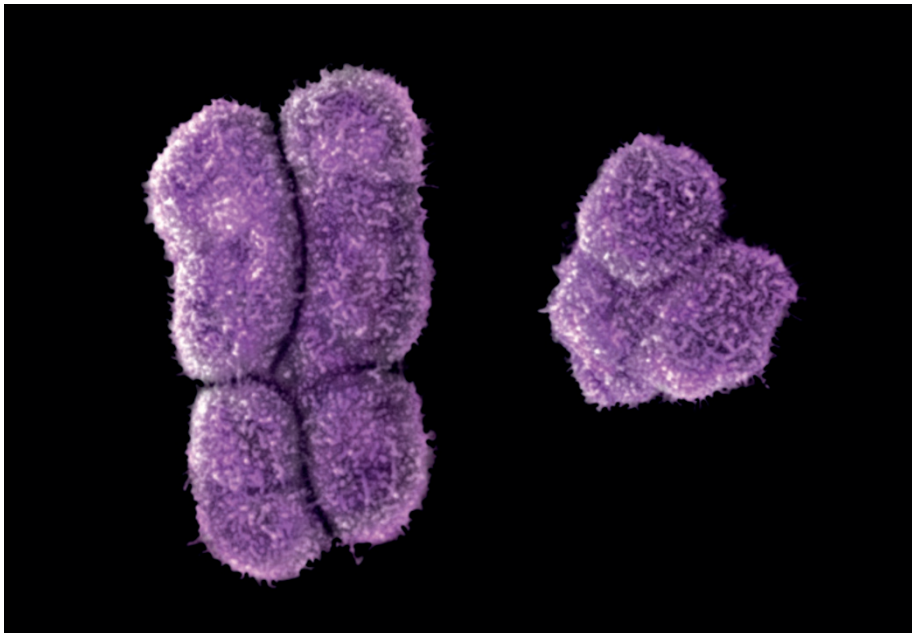
of four placental mammals (rat, mouse, bull and marmoset) and the marsupial opossum. They compared these with existing sequences for another three placentals (rhesus macaque, chimpanzee and human). Of the 184 genes that the authors infer to have been on the ancestral sex chromosomes some 300 million years ago, they find that only 3% survive on the Y chromosome of one or more of these mammals (Fig. 1).

Consistent with previous reports, this means that massive degeneration and gene loss did occur early in the history of the mammalian Y chromosome. However, once the genes had run this gauntlet, those that remained enjoyed remarkable stability on the Y chromosome. The authors also find that the 36 genes that are present on both the X and the Y chromosomes of all eight species they examined have maintained a stable presence for the past 25 million years. Ten genes were found to be shared across the Y chromosomes of the tammar wallaby, the Tasmanian devil and the opossum, indicating a stable Y-chromosome presence for the 78 million years of the marsupial lineage. These findings have important implications for our understanding of how natural selection acts to retain active functioning of specific subsets of genes on the Y chromosome.

Cortez *et al.* took a faster survey approach, in which they sought RNA molecules that are expressed in males but not females and then verified that the genes encoding these RNAs are found only in male genomic DNA. This allowed them to identify 134 genes transcribed from the Y chromosome across 10 mammals and to follow their evolutionary fates. By including the chicken (in which males have two Z chromosomes and females have one Z and one W chromosome) and the platypus (a monotreme that has a bizarre array of five X and five Y chromosomes), the authors were able to paint a broader picture of sex-chromosome evolution. Most noteworthy is their observation that the sex chromosomes of placental mammals, birds and monotremes had essentially independent origins, which means that patterns of gene loss and of specific retention of classes of genes on their Y (or W) chromosomes can be compared.

These data add depth and confidence to the model of evolutionary 'strata' on the sex chromosomes[6] that mark the time points at which X and Y sequences ceased recombining and subsequently diverged. Intriguingly, despite their independent origins, the authors find that the oldest strata in placental mammals, monotremes and birds are remarkably similar in age, estimated to have occurred 181 million, 175 million and 137 million years ago, respectively.

Another key aspect of genes on sex chromosomes is dosage sensitivity. Dosage-insensitive genes are those that function perfectly well when present as a single copy, and these are especially likely to become X- or Y-specific. By contrast, two copies of dosage-sensitive genes are required for normal health, and such genes are likely to be retained on both the X and the Y chromosome[7]. Genes involved in regulating gene transcription — such as those that encode transcription factors — commonly function inadequately in only a single dose, providing a hypothesis for why the Y chromosome has retained genes involved in transcription regulation.



POWER AND SYRED/SPL

Figure 1 | Small but stable. The human Y chromosome (right) is much smaller than the X chromosome (left), as a result of extensive degeneration early in Y-chromosome evolution. However, comparisons with other mammalian Y chromosomes by Bellott *et al.*[3] and Cortez *et al.*[4] show that there has been remarkable gene stability across Y chromosomes following this initial gene loss.