Evolutionary biology

Chromosome chain makes a link
Laura Carrel

The platypus’s sex chromosomes are as peculiar as its appearance. Five X and five Y chromosomes form a remarkable chain-like configuration in male reproductive cells that ensures appropriate sperm formation.

An Australian Aboriginal legend proposes that the platypus is the offspring of a duck and a water-rat, with a duck-like bill and webbed toes, but four feet and fur like a rat. However, despite some avian and reptilian features, phylogenetic studies classify the platypus as a monotreme, an egg-laying mammal. Monotremes diverged from the rest of the mammalian lineage some 210 million years ago, and examining them not only gives a unique evolutionary perspective to biological processes specific to mammals, but also provides links to more distant animals, such as birds.

One example of this is provided by studies of platypus chromosomes, described in this issue (page 913), and in Proceedings of the National Academy of Sciences, by members of the same groups. The reports clarify the composition and behaviour of platypus sex chromosomes, and challenge current theories on the evolution of sex determination.

Sex chromosomes and sex-determining genes differ among organisms (Fig. 1, overleaf). In most mammals, females have two homologous sex chromosomes, and males have an X and a Y. The Y chromosome harbours a sex-determining gene, SRY, that functions as a master switch, initiating a developmental programme that directs the embryonic gonad to form a testis rather than an ovary. However, sex determination seems to have evolved independently in some organisms. In birds, for example, the females are the ones with two different sex chromosomes, designated ZW, whereas males have ZZ. Birds have no SRY gene, but a candidate tests-determining gene called DMRT1 occurs on their Z chromosome (Fig. 1). Although monotrems might be expected to have a similar system to other mammals, they lack SRY and, until now, even the composition of sex chromosomes in the platypus was poorly understood.

Early studies of platypus male reproductive cells undergoing meiosis, the specialized cell division process that creates sperm, showed that a group of chromosomes were linked in an unusual chain-like configuration. A similar meiotic structure occurs in a few disparate organisms, such as evening primrose and termite, but it has not been seen before in vertebrates. Grützner and colleagues have created fluorescent ‘paints’ for individual platypus chromosomes. By tagging the chromosomes in this manner, they could determine the number of copies of each chromosome in males and females, and their order in the male meiotic chain (see Fig. 2, in the future. Highly pathogenic strains of avian influenza have in very recent times crossed from birds to humans. As virologists Richard J. Webby and Robert G. Webster have put it (Science 302, 1519–1522; 2003): “An old foe has again raised its head, reminding us that our worst nightmare may not be a new one.”

How easy would it be to control a new influenza pandemic? By analysing data on deaths from pneumonia and influenza in 45 US cities during 1918, Mills et al. estimate the reproductive number (R), that is, the number of secondary cases produced by each primary case. This is a measure of viral transmissibility, and given the rapid spread of the 1918 pandemic one might expect it to be rather high. But it turns out that its transmissibility was actually quite modest, with each primary case giving rise on average to just three or four secondary cases.

In the absence of global stocks of antiviral drugs and vaccines, warn the authors, control of a similar influenza strain would probably require aggressive measures early in an outbreak to reduce contacts between persons, whether or not they had already been diagnosed with flu. If a variant virus cropped up with a similar pathogenicity but a much higher transmission rate, we could be in for real trouble.}

Rory Howlett
news and views

![Comparison of sex chromosomes. The four groups represented are birds (the chicken) and examples (human, kangaroo and platypus) of three orders of mammal. The time when each species diverged from their common ancestor is indicated in millions of years (Myr) ago. Pink indicates similarity between X chromosomes; blue, similarity to the Z chromosome. As only one gene from the bird Z chromosome has been mapped to platypus X5, it is not known whether the platypus chromosomes have other regions that resemble the Z chromosome.

Figure 1](image)

Such high segregation fidelity of this complicated structure seems remarkable, particularly given that abnormally rearranged chromosomes in other species, in which just two (not five) pairs of chromosomes physically associate at meiosis, frequently result in chromosomes separating unequally or even cause the cells to stop dividing. Perhaps the physical constraints of this large chain make alternative segregation patterns less probable. It is possible that, as hypothesized for a similar structure in evening primrose, the platypus chain forms a ‘zipper’ that introduces tension to facilitate segregation of alternate chromosomes. But further studies are required to elucidate the mechanism of separation.

Sex chromosomes (in birds or mammals) are thought to have evolved from a pair of non-sex chromosomes1. A series of chromosome rearrangements allowed the X and Y (or Z and W) to evolve independently. The present mammalian Y is a small chromosome with few genes, and the significantly larger X is highly conserved among mammals (Fig. 1), as its evolution has been influenced by X-chromosome inactivation. This is a chromosome-wide gene-silencing process that equalizes gene dosage between males and females.

The platypus meiotic chain probably formed from a succession of additional rearrangements between sex chromosomes and non-sex chromosomes. Models predict that the ancestral sex-chromosome pair is actually X1,Y1 because, unlike X1,Y2, they are not very similar to one another, suggesting that they had long diverged. Grützner et al.2 also found that platypus X5 contains a close relative of the bird candidate sex-determining gene DMRT1. Although they acknowledge that DMRT1 is an unlikely testis-determination gene in platypus, because it is present in two copies in females and only one in males, the authors argue that the significance of this location is in anchoring components of the mammalian X chromosome and bird Z chromosome at either end of the meiotic chain. These data raise the intriguing possibility that, contrary to previous theories3, the bird and mammalian sex-chromosome systems are somehow linked. Additional comparative mapping will be necessary to test this hypothesis. The chromosome paints developed here will be a valuable resource for exploring the origins of the chromosomes involved. One might expect that the platypus sex chromosomes will show additional bird Z- and potentially even W-chromosome similarity.

This work raises many questions. First, with the two most obvious candidates, SRY and DMRT1, eliminated, the search for the platypus sex-determination gene must continue. Its identification could be important for understanding sex determination in other mammals that lack SRY4. Another key question is whether the platypus Xs are dosage compensated, because Grützner et al.2 show that only a subset of X1–5 sequences are present on Y1–5. Although X5 seems to be dosage compensated5, it is unclear whether the mechanism is similar to X-chromosome inactivation in other mammals.

Further studies of the curious meiotic chain in this odd duck of a mammal will provide insights into the evolution of chromosomes, meiosis and sex determination. Who knows what additional links this chain of sex chromosomes will establish?

Laura Carrel is in the Department of Biochemistry and Molecular Biology, Pennsylvania State University College of Medicine, Mail Code H171, Hershey, Pennsylvania 17033, USA.

e-mail: laurac@psu.edu