

# The Platypus or the Egg?

BY STEPHEN LUNTZ

**The sequencing of the platypus genome promises to shed light on mammalian evolution as well as the strange physiology of this egg-laying, venomous, duck-billed, beaver-tailed mammal.**

Dr Russell Jones describes the platypus as “our most distant mammalian relative”. Consequently, in an era when the sequencing of animal genomes has become common, the announcement of the first monotreme genome to be sequenced has aroused more than the usual excitement.

Jones, of the University of Newcastle’s School of Environmental and Life Sciences, is one of more than 100 scientists around the world who took part in the platypus genome project. “Mapping the entire genetic record of the platypus is critically important to understanding the evolution of mammals and humans,” he says. “If you look back more than

160 million years you will find the last common ancestor between humans and the platypus.”

The sequencing was announced on 8 May as the cover story in *Nature*, and attracted plenty of attention. “The platypus genome will allow us to examine the evolution of mammalian-specific characteristics such as warm bloodedness, lactation and genomic imprinting,” says Dr Andrew Pask, a co-author of the *Nature* paper from the University of Melbourne’s Department of Zoology.

Prof Jennifer Graves, director of the Centre of Excellence for Kangaroo Genomics, describes the platypus as “probably the most keenly awaited genome since the chimp because platypuses are so weird,” but says that “the platypus is not an evolutionary intermediate. The platypus is a platypus. But it’s the comparisons of humans with the platypus that can tell us about the fork in the road when the platypus went one way and we went another way.”

Graves says that the platypus genome reflects the extraordinary mixture of mammal-like and reptile-like features of the animal. “For instance, the genome contains genes that make the complex mixture of proteins in milk, so we know that lactation was invented before the platypus diverged from other mammals 166 million years ago,” she says.

“But at the same time there are genes that make egg yolk proteins – although there is only one of the three that are present in a bird – and genes that make the toxins in the unique platypus venom which are similar to those in snake venom but evolved independently.

“In addition, there are genes that reflect some of the unique characteristics of the platypus, such as a huge repertoire of vomeronasal receptors that evidently help the platypus to sense its prey under water.”

## THE VENOMOUS MAMMAL

The day before the platypus genome was published, a paper in *Genome Research* identified three genes responsible for the venom produced in the male platypus’ hind spur. “Venom in a mammal is unusual,” says Dr Kathy Belov of the University of Sydney’s Faculty of Veterinary Science, “and we wanted to see where these genes came from and whether they are related to venom in snakes and lizards”.

Decoding of the genes involved in the production of platypus venom has potential applications in pain relief and antibiotic medication. This may seem counterintuitive since the terrible pain caused by platypus venom cannot be relieved with painkillers, but it is exactly why Belov says it is worthy of study.

“We don’t know how the venom



Jenny Graves announcing the sequencing of the platypus genome at the Australian Science Media Centre. Photo: Richard Timbury



works,” she says. “It causes a huge amount of pain that morphine can’t control. We think if we can understand how this works we’ll know more about pain responses and how to control them.”

The pain from a platypus sting can last months, during which the suffering limb is nearly paralysed, but Belov says we also don’t know how it is that it gradually eases away. However, now that three genes for venom production have been identified Belov says “we’re talking to people” about efforts to express the venom proteins for further study.

Belov says that the platypus “recruited similar genes to make venom as snakes, but this occurred independently”. This provides great opportunities for comparative research. “There’s obviously something important about the genes recruited,” she says.

Another potential application for platypus research lies in antibacterial products to combat drug-resistant bacteria. Belov says: “When they’re young, platypus have no protection,” because their immune systems don’t get to develop during gestation like ours. “Yet

they live in these burrows full of mud and bacteria. We suspect the antimicrobial factors are passed through the milk.”

However, the connection of the venom to genes that are essential to the immune system has made the venom genes a particularly attractive target for further research.

### SEX SELECTION

Another area in which the platypus has proven remarkable is in sex selection. “To our surprise we discovered that the platypus X and Y chromosome are completely unrelated to the X chromosome of all other mammals,” says Dr Paul Waters of the Centre for Excellence for Kangaroo Genomics. “Platypus sex chromosomes share extensive similarity to the sex chromosomes of the distantly related birds, suggesting that our ancient mammal-like reptile ancestor might have had sex chromosomes more like those of the current-day birds.”

News of this finding broke before the paper’s publication (*AS*, May 2008, p.10). Graves describes this as “the biggest surprise for me”.

While the system may be more like birds than mammals, the platypus method for determining sex is nevertheless unique. Most animals have just two sex selection chromosomes, and the most known is four. However, platypuses have 10 sex chromosomes, which would seem to complicate life to an extraordinary extent without offering any obvious advantages. Researchers are still getting their heads around how the many platypus sex selection chromosomes operate as well as any evolutionary benefits they may confer.

During sperm production the five X-chromosomes all go to one cell and the five Y-chromosomes to another. The researchers confirmed that prior to this split the chromosomes line up in a defined pattern  $X_1Y_1-X_2Y_2-X_3Y_3-X_4Y_4-X_5Y_5$ . If this process did not occur one would expect hermaphroditic platypuses to be common, but it is still hard to imagine how such a process evolved.

### A SLOWLY EVOLVING SPECIES?

Fossil evidence from a platypus ancestor suggests that the species has changed little in the past 110 million years or more (*AS*,

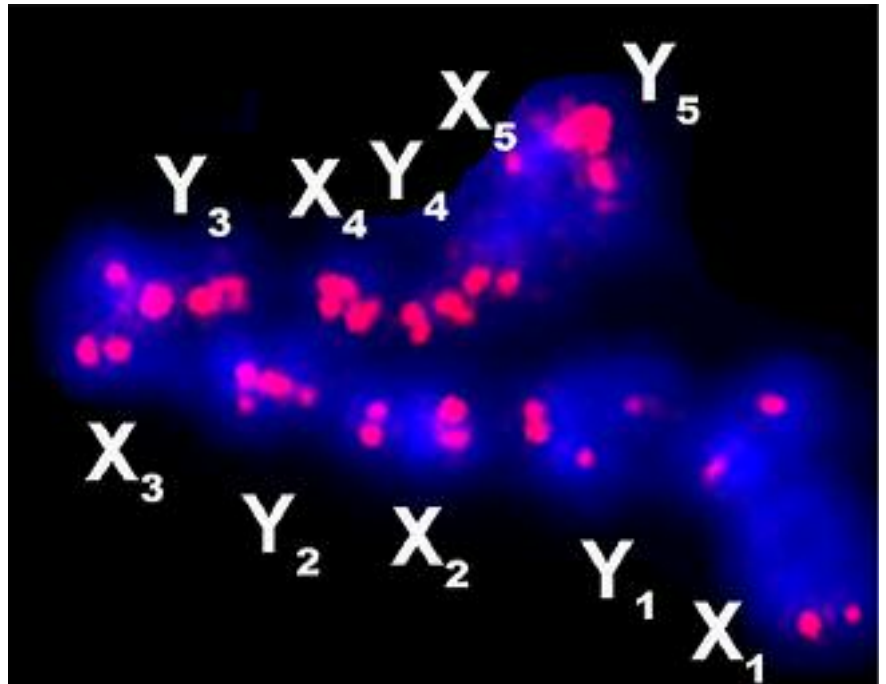
May 2008, p.10). “It’s an interesting question whether the platypus genome has evolved more slowly than other mammals,” Graves says. “A lot of people assume this is so because they still lay eggs and have eye and skeletal structures like reptiles. However, the measures of base substitution show that, on average, genes have evolved at about the same rate as in humans.”

Dr Sarah Munks of the University of Tasmania’s School of Zoology says that in all the attention paid to the monotreme’s mix of mammalian and reptilian characteristics it should be noted there are also “features that are unique to the platypus. These unique features are reflected in its ecology and behaviour, enabling the platypus to have survived for millions of years in its freshwater habitat on our dry continent.”

However, while these characteristics have served the platypus well over millions of years, their lack of flexibility is proving a modern-day problem. “Our understanding of the platypus’ status is very much hampered by how difficult these animals are to census accurately,” says Dr Melody Serena of the Australian



PhD student Camilla Whittington was lead author of a paper in *Genome Research* investigating the content of platypus venom.



The platypus has an unrivalled five sets of sex chromosomes.

Platypus Conservancy. “The past decade of drought in south-eastern Australia has certainly reduced platypus numbers in many areas. The species is also under pressure from widespread habitat degradation, water pollution and mortality due to animals becoming entangled in litter or drowning in illegal fishing nets.”

### MISSED OPPORTUNITIES

Having been isolated from evolutionary processes elsewhere in the world for 80 million years, Australia has access to a unique set of animal and plant genomes. Yet while most platypus research occurs in Australia, and one-quarter of the co-authors of the *Nature* paper are Australian, the platypus genome project could not have proceeded without the significant backing of overseas researchers.

Australians may have initiated the sequencing proposal, supplied the DNA and helped interpret the sequence, but the actual sequencing was done in the United States. This follows the sequencing of the eucalypt genome in Japan, while a South American opossum beat the Tamar wallaby to be the first marsupial sequenced.

Federal government support has been

almost entirely absent for genetic sequencing in Australia, and sequencing of the kangaroo genome is only occurring because the US National Institutes of Health matched a grant from the Victorian State Government.

“Does it matter that Australia is not a contributor in genomics?” Graves asks. “The data all goes up on the web anyway, so can’t we all sit on our bums, then get it for free?”

“No. Not in the long-term anyway. Unless we have a seat at the genomic table, we won’t be seriously involved in the next stage, the mad rush to use the avalanche of data to invent new diagnostic tools, new drugs, new approaches to agriculture.”

Canada is similar in size to Australia yet has put CA\$840 million into genomics over 10 years. If Australia followed the Canadian example there would be no shortage of local species to study.

So far no coral genome has been sequenced, and Dr Walt Dunlap of the Australian Institute of Marine Science argues that this is a major obstacle to our capacity to fight the effects of global warming and ocean acidification on coral reefs.