Photo: Ian Elton

The Platypus Inheritance

BY ANN MOYAL

Sequencing of the platypus genome has brought new insights into mammalian evolution, but Australian scientists are concerned that funding for research into this unique animal may dry up.

For Australian geneticists, molecular biologists, microbiologists, veterinary and evolutionary biologists, biochemists, immunologists, physiologists, zoologists, ecologists, palaeontologists and a host of other multidisciplinary scientists, nothing could be more compelling than the avalanche of data that has flowed from the publication of the platypus genome last year (*AS*, July 2008, pp.24–26).

The first Australian animal to be included in the Human Genome Project – which extended during the 1990s to over 30 species of mammals – the platypus has topped the biological chart in its revelations and in the promise of what the data can tell us about the genetic processes, interrelationships and survival strategies of monotreme and mammalian evolution and their significance for human kind. Australia's faunal icon has emerged in this new era of biotechnology uniquely placed in its genetic composition as a comparative tool for studying mammalian evolution.

Over the past 200 years we have grown only slowly in our knowledge of *Ornithorhynchus anatinus*. Seemingly embracing several parts of other animals, this semi-aquatic monotreme is a furred, duck-billed mammal that lays eggs, nourishes its young with milk rich in fats, sugars and proteins, has male venomous spurs and, reaching back over more than 150 million years of evolutionary time, has survived as the oldest living mammal in Australia.

From the moment the first dried specimen reached England in 1799, the platypus has occupied a central place in the biological world. Amid British and French wrangling, this "paradoxical quadruped" was variously figured as possibly (or contentiously not) a milk-producing mammal that, alternatively, gave birth to live young, hatched its young from eggs fully formed within its body, or actually laid eggs.

It was not until 1884, nearly 90 years after the first well-preserved specimen reached the Royal College of Surgeons in London, that an intrepid young researcher from Cambridge, carrying out research on Queensland's Burnet River, managed to kill a female platypus who had just laid one egg and held a second egg at the mouth of her uterus. Off went the famous cable – "monotremes oviparous, ovum meroblastic" – to inform a gathering of international biologists meeting in Montreal that year that this mysterious creature actually laid soft-shelled eggs that were absorbed as food by the developing young, like a bird. Fur from eggs!

Despite rising research on its physiognomy and ecology, the platypus has held many secrets and it was not until the mid-1990s that a group of researchers from Monash University and the Australian National University discovered that it was furnished with a unique system of electroreception and electrolocation in its bill that enables it, with ears, eyes and nostrils firmly closed, to avoid obstacles and locate its invertebrate food supply underwater, a finding ranked as one of the major natural history discoveries of the time.

Now this enigmatic monotreme has stolen the scientific limelight again.

Working laboriously from old methods, ANU researchers and their Cambridge collaborators had managed by the 1990s to isolate only 23 genes from the platypus genome. Now, in a dynamic new era of gene technology, the platypus genome study has exposed more than 18,000 genes of enormous significance to biological research. Of these, the platypus shares 82% with humans, dogs, opossums and chickens.

But mapping revealed that there was no homology between the platypus sex chromosomes and the XY pairs of other mammals. An international team led by Dr Frank Grutzner of the University of Adelaide had already unveiled the platypus' 10 sex chromosomes, the most complex sex determination system seen in any vertebrate. Now the genome project has vastly multiplied this evidence and confirmed that these show strong linkages to bird chromosomes, suggesting that the monotreme's sex chromosomes derive from an ancient reptile system.

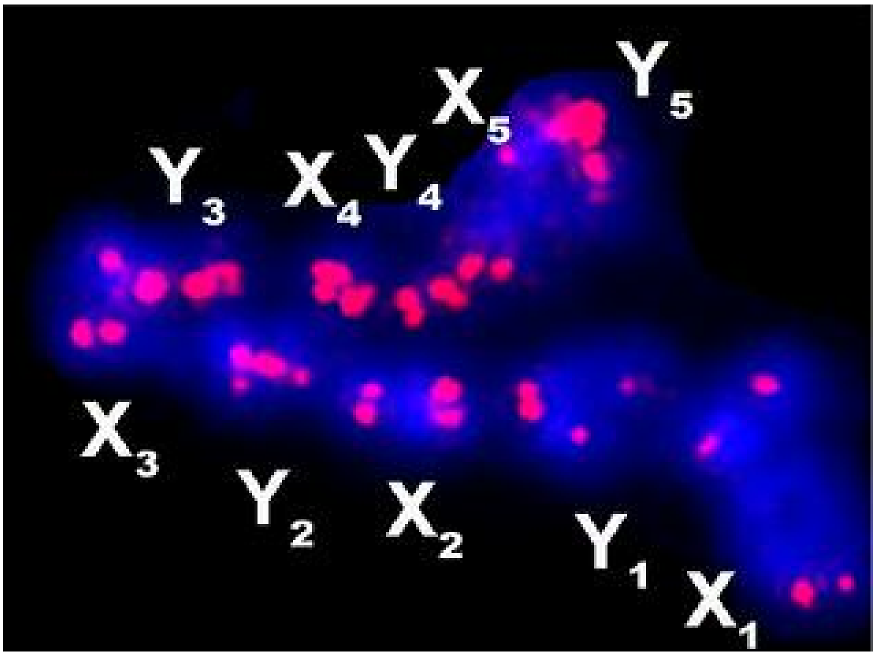
"We expected the genome to be weird, and it certainly is," said Prof Jenny Graves of ANU's Comparative Genomic Research Group, who first put forward the platypus for the genome study. The study, however, has provided "a unique signature of evolution". Essentially the platypus genome revealed a fork in the evolutionary road about 166 million years ago when the platypus went one way while human and other placental animals went another.

The genetic lineage confirms the outstanding evolutionary success of this Australian animal, positioning it as a "missing link" between the two epochs of reptilian and mammalian preeminence. The platypus can thus be seen as the last common ancestor of extant mammals or, as Dr Elizabeth Murchison of the ANU more inclusively frames it: "The monotremes, with only the platypus and four species of echidna as extant members, represent the basal branch of the mammalian lineage". '

"Given the fact that 99% of all mammalian species to ever exist are extinct, it is fortunate to have a mammal/reptile relic alive, well and available," says Stephen O'Brien, Chief of the US National Cancer Institute's Laboratory of Genetic Diversity.

Prompted by this new wealth of data, a large contingent of multidisciplinary Australian and international scientists converged on Victor Harbour, South Australia, in late November 2008 for the Australian Academy of Science's 2008 Boden Research Conference, *Beyond the Platypus Genome*, to discuss work-in-progress and offer cross-disciplinary analysis.

Important early research addressed the character of the once historically contested question of the platypus' mammary gland, its milk and the process of lactation. Now Christophe Lefèvre and his associates at Deakin University, using comparative studies of caseins (milk proteins precipitated by lactic acid), have



The platypus has an unrivalled five sets of sex chromosomes.

indicated that the monotreme mammary gland represents an ancient form of mammary tissue that predates the evolution of eutherian mammary gland structure. Thus the monotremes provide particular insights into the ancestral drivers for lactation and how these have adapted in different lineages, including our own. This signifies that one of the genetic innovations that led to the development of milk occurred more than 166 million years ago after mammals first split from the lizard-like predecessors that gave rise to modern reptiles and birds.

Other research has focused on the platypus' venom, which is produced in the male's hind leg spur during the breeding season and used against other males to assert dominance. Genome project researchers found that the poison produced by the platypus arose independently from the poisons of reptiles and snakes during the evolution of their venom many millions of years ago. Platypus venom contains a cocktail of more than 50 different substances in which at least three kinds of peptides play crucial roles. Studies unfolding on the potent pain-inflicting venom offer the prospect of new painkillers and antihypertensives.

At the same time, cross-disciplinary research being conducted at the University of Sydney by teams headed by biochemist Philip Kuchel and veterinary scientist Kathy Belov suggest that some components of the innate immune system of the platypus appear to have evolved from antimicrobial genes known as defensins, and have been recruited for specialised functions in the venom. Since the venom is a complex mix of components, it has provided a unique insight into the biochemistry of this so-called "primitive" mammal.

A further outcome of the conference was the increased understanding of Australia's second monotreme, the echidna. Papers attested to the rising interest and importance of echidna research and the relevance of the echidna's future inclusion in the genome project.

One unexpected message on the monotremes emerged from the conference. "We thought that we have platypus and echidna. Now we learn that there are some very significant genetic, ecological and physiological differences depending on whether you look at an echidna from Tasmania or King Island, or a platypus from Queensland and a platypus from New South Wales," Grutzner said. The assembled platypus genome data already offers the potential to carry out more intimate analyses of population structure and genetic diversity using genetic markers that will contribute significantly to future management plans for the long-term conservation of the platypus. Such prospects have large implications for the four species of echidna.

Overall, the span of conference studies provided major pointers to understanding how fundamental mammalian biological processes have evolved, including some singularly innovative survival strategies of the platypus. As Prof Jae-il Park from Stanford University underlined: "The genome information is like a time-lapse recording of our natural history, and the recent explosion of the genome database is giving us the missing frames – the ones that show how novel genes were created and lived and how the change occurred during natural selection".

But there is serious concern about the critical necessity for future funding of monotreme research in Australia. The enormous evolutionary distance of the platypus from other mammals had itself made assembly and annotation of its genome a major challenge. Now research across a range of genetic, biological, molecular, biochemical, veterinary, physiological, medical, statistical, palaeontological, comparative genomics and other fields indicates the singular importance of a collaborative focus.

The 2008 Boden Research Conference was the first to draw high profile international researchers to its monotreme context, and proved to be the most important monotreme assembly yet convened . This, then, is surely the time to call both for increased government support for this crucial research in Australasia and to present a unique opportunity for major, earmarked monotreme research funding from private sources.

Ann Moyal is a leading historian of Australian science and the author of *Platypus: The Extraordinary Story of How a Curious Creature Baffled the World* (Allen & Unwin, 2001).