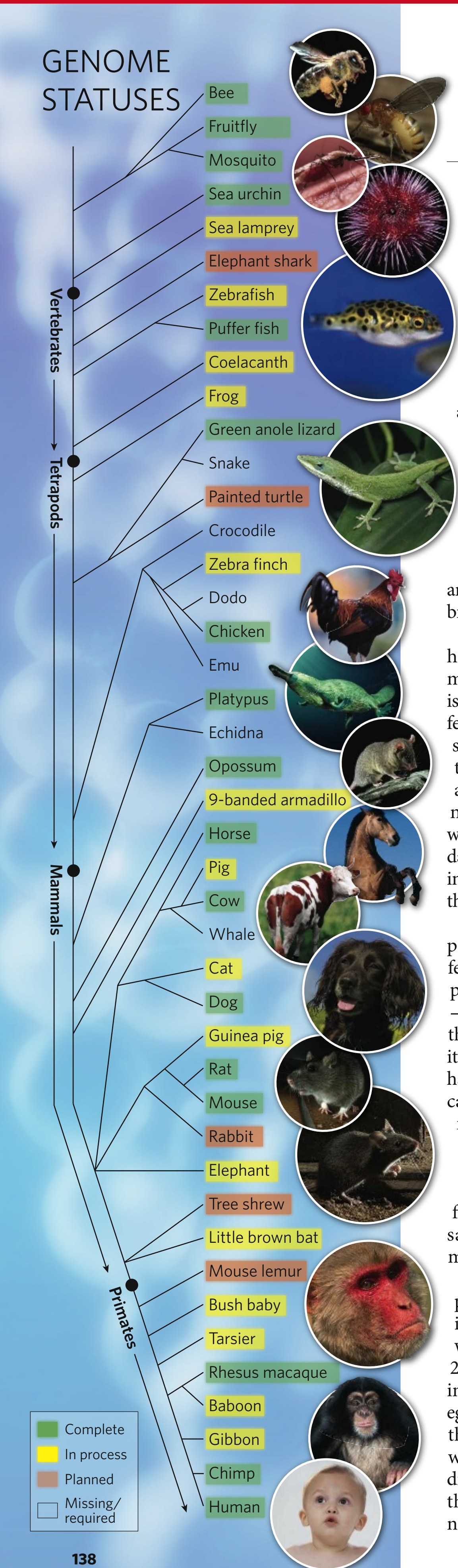

NEWS

Top billing for platypus at end of evolution tree

A draft sequence of the platypus genome reveals reptilian and mammalian elements and provides more evidence for its place in the ancestral line of animal evolution.

The platypus (*Ornithorhynchus anatinus*) is endemic to Australia and one of nature's oddest creatures, seemingly assembled from the spare parts of other animals. The semi-aquatic monotreme is a venomous, duck-billed mammal that lays eggs, nurses its young and occupies a lonely twig at the end of a sparse branch of the vertebrate evolutionary tree.

Now, the structure of its genome has revealed new clues to how mammals evolved. "The analysis is beginning to align these strange features with genetic innovation," says Wesley Warren of Washington University in St Louis, Missouri, the lead author of the genome analysis — a huge international project (see page 175). Comparisons with the genomes of other mammals will help to date the emergence of the platypus's distinguishing characteristics and reveal the genetic events that underlie them.

"There is nothing quite as enigmatic as a platypus."

For example, mammals are defined by their possession of mammary glands, which in females can produce milk. Although the platypus doesn't have nipples, it produces true milk — full of fats, sugars and proteins — which the young suck through a glandular patch on its skin. The analysis shows that the platypus has genes for the family of milk proteins called caseins, which map together in a cluster that matches that of humans. This is a sign that one of the genetic innovations that led to the development of milk occurred more than 166 million years ago, and after mammals first split from the lizard-like sauropsids that gave rise to modern reptiles and birds.

The genes relating to the platypus's eggs offer further insight. The embryos develop within the maternal uterus for 21 days before they are expelled in a thumbnail-sized leathery egg. After 11 days of incubation, the young hatchlings emerge with their organs not yet fully differentiated. Like marsupials, they finish developing while nursing. The platypus shares with other mammals four genes associated with the zona pellucida, a gel-like coating that facilitates fertilization of the egg. But it also has two matches for *ZPAX* genes that had previously been found only in birds, amphibians and fish. And it shares with the chicken a gene for a type of egg-yolk protein called a vitellogenin. That suggests that vitellogenins, which are found in birds and fish, predate the split from the sauropsids, although the platypus retains only one vitellogenin gene, whereas the chicken has three.

Other characteristics that seem purely reptilian turn out to have evolved independently, the analysis suggests. Male platypuses have spurs on their hind legs that are loaded with a venom so potent it can kill a dog. Like the venom of reptiles, the poison is a cocktail of variations on at least three kinds of peptide. But the variations arose from duplications of different genes in platypuses than in modern reptiles. The similarity in venom is an example of convergent evolution between the two tetrapods.

"There is nothing quite as enigmatic as a platypus," says Richard Gibbs, who directs the Human Genome Sequencing Center at Baylor College of Medicine in Houston, Texas. "You have got these reptilian repeat patterns and these more recently evolved milk genes and independent evolution of the venom. It all points to how idiosyncratic evolution is."

The sex of the platypus is determined by a set of ten chromosomes, an oddity that sets it apart from all other mammals and from birds. These chromosomes link during meiosis to form a chain that ensures every sperm gets a set of all Xs or all Ys. Despite the similar designations,

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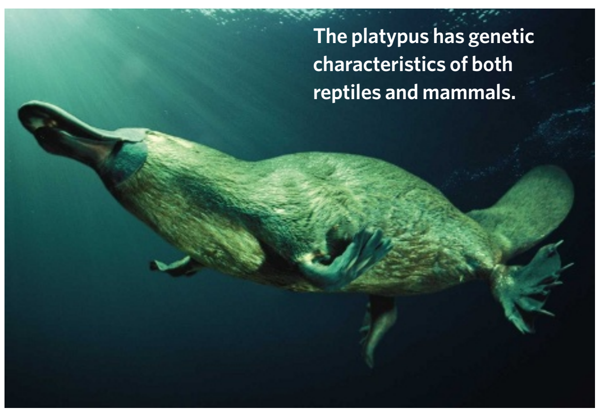
The platypus has genetic characteristics of both reptiles and mammals.

D. WATTS/NATUREPL

none of the platypus X chromosomes resembles the human, dog or mouse X. "The sex chromosomes are absolutely, completely different from all other mammals. We had not expected that," says Jennifer Graves of the Australian National University in Canberra, who studies sex differentiation and is an author on the paper. Instead, the platypus Xs better match the avian Z sex chromosome. Another chromosome matches the mouse X, Graves and her colleagues report in *Genome Research* (F. Veyrunes *et al. Genome Res*. doi:10.1101/gr.7101908; 2008). This is evidence that placental mammalian sex chromosomes and the sex-determining gene *Sry* — found on the Y chromosome — evolved after the monotremes diverged from mammals, much later than previously thought. "Our sex chromosomes are a plain old ordinary autosome in the platypus," Graves says.

A team led by Gregory Hannon of Cold Spring Harbor Laboratory in New York sequenced microRNAs, which regulate gene expression, that were isolated from six platypus tissues. Again they found a mix of reptile and mammal examples (E. P. Murchison *et al. Genome Res.* doi:10.1101/gr.73056.107; 2008). "We have microRNAs that are shared with chickens and not mammals as well as ones that are shared with mammals, but not chickens," Hannon says.

"The reptilian characteristics [of miRNA] are not convergent features, and this is a feature of the genome as well," Hannon says. "Morphology didn't have to be reflected at the level of molecular biology, but in this case it was."

Adam Felsenfeld, who directs the Large-Scale Sequencing Program at the US National Human Genome Research Institute in Bethesda, Maryland, says: "I find it fascinating that genomic features of what are now two separate lineages can coexist in the genome of a single organism."

About half of the platypus genome contains non-coding DNA sequences. Many are 'interspersed repeats', copies of transposable elements that are characteristically abundant in other mammalian genomes. In contrast, repeats of very short sequences called microsatellite DNA are rarer in the platypus genome than in other mammals' and more closely resemble those of reptiles, with the balance of nucleic acids tipped toward A–T base pairs.

The sequence information has already generated useful genetic markers for studying the population structure of the elusive platypus in the wild. Differences in repeated elements, for example, separate the Tasmanian population from that on Australia's mainland, and could be used to improve understanding of the ecology of this enigmatic animal. There are as yet no plans to sequence the genome of its closest relative, the echidna. ■

Susan Brown

D. PELED/AP PHOTO

PLATYPUS PLUS
Watch a video interview or listen to the podcast.
www.nature.com/news

Chemists spin a web of data

A chemist running a computer server from his home is quietly solving one of his colleagues' biggest frustrations by providing the community with an open-access source of chemical information.

Although biologists have enormous public databases of genes and proteins, chemists usually have to pay for access to data on molecules. Chemist Antony Williams is hoping to change this in a move likely to ruffle the feathers of the American Chemical Society. Williams, a private consultant based in Wake Forest, North Carolina, has started a website called ChemSpider that has compiled data on nearly 20 million molecules in a year.

The modest project has made chemists interested in open access take notice — last week, the number of daily users of the site surpassed 5,000. "It's quite an exciting development," says David Wild, a chemical informatics researcher at Indiana University, Bloomington, who uses the service. "ChemSpider is working to integrate information in a unique way."

Chemical data have long been available, but at a hefty price. The largest supplier of such information is the American Chemical Society's Chemical Abstracts Service. The service, which is more than a century old, includes data on roughly 35 million molecules. But university and industry chemists must pay thousands of dollars to use the database. The society will not reveal numbers, but fees for using the database are thought to make up a substantial portion of its US$311-million annual income from 'electronic services'. Some have been highly critical of the society's grip on chemicals.

In recent years, several public sources for chemical information have appeared on the scene. The largest, PubChem, is run by the National Library of Medicine in Bethesda, Maryland, and contains data on some 19 million chemical structures. But PubChem's data focus on biological information, according to Williams. Other potential sources of information, such as Wikipedia, lack the algorithms needed to search chemicals according to their structure. "I noticed there was this gap," says Williams. "So I decided to try an experiment."

Rather than building up a database, the ChemSpider service scans open-access sources, including PubChem and Wikipedia, for chemical data. It compiles the publicly available information in a single location, and allows users to follow links to the original source material. The site is maintained with modest profits from advertising and the work of about 30 active volunteers who double-check the data pulled in from outside.

E. KOCH/ZEFA/CORBIS

Chemical data are becoming more freely available.

The site is not without its flaws. "There's an awful lot of chemical information, but there's an awful lot of rubbish as well," says Barrie Walker, a retired industrial chemist in Yorkshire, UK, who helps maintain the site. When working with such a large database, he says, "you're bound to end up with a quality issue". Williams adds that the site still has problems with certain searches. For example, it struggles to distinguish between isomers: molecules with the same chemical formula arranged in different structures.

But Williams nevertheless believes that the service may be able to compete with for-profit services. "What I'm doing is highly disruptive," he says. "I think it can be done and it needs to be done." The American Chemical Society declined to comment on ChemSpider. ■

Geoff Brumfiel