

## OBESITY

## Fat chance

Eat more, move less and lose weight — sounds too good to be true. Yet this is exactly what Julia Fischer and her colleagues observed in mice lacking one specific gene (J. Fischer *et al.* *Nature* advance online publication doi:10.1038/nature07848; 2009).

Obesity is a complex disorder because, as well as environmental factors, many genes seem to be involved. One such gene is *FTO*, as several studies have indicated that different versions of *FTO* are strongly correlated with body mass index: individuals carrying the high-risk version weigh roughly 3 kilograms more than those with the low-risk version.

Fischer *et al.* studied mice lacking *FTO* (*FTO*<sup>-/-</sup> mice) and

compared them with normal mice and with those carrying only one copy of the gene (*FTO*<sup>+/-</sup> mice). The absence of *FTO* did not affect embryonic development, but by six weeks after birth, *FTO*<sup>-/-</sup> mice weighed on average 30–40% less than normal or *FTO*<sup>+/-</sup> mice. This reduction in weight was associated with a marked loss of white fat tissue, with near-complete loss by 15 months.

The lower weight of the mutant mice doesn't seem to be due to reduced calorific intake. In fact, these mice ate more in proportion to their body weight than normal mice. Moreover, on a high-fat diet, both groups of mutant mice gained much less weight than normal animals. Instead, *FTO*<sup>-/-</sup>

mice used more energy, while not moving much. The authors suggest that this increased energy expenditure might be due to higher activity of the sympathetic nervous system — that is, to enhanced circulating levels of adrenaline and noradrenaline.

Fischer and colleagues' data indicate that variations in the human *FTO* gene might affect its levels of expression, either putting individuals at risk of obesity or protecting them from it. It remains to be seen how *FTO* might regulate the activity of the sympathetic nervous system.

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jawed vertebrate morphology. This is where the evidence for internal fertilization and live-bearing in placoderms becomes important.

The ancestral mode of reproduction for osteichthyans seems to be external fertilization. The distribution of live-bearing among living vertebrates strongly suggests that internally fertilizing live-bearers are unlikely to give rise to externally fertilizing spawners, so we would not expect the osteichthyan stem lineage, or the gnathostome stem lineage below it, to contain a segment characterized by live-bearing. Brazeau's analysis<sup>7</sup> places the ptyctodonts and arthrodires as successive branches off the gnathostome stem, implying the existence of such a segment unless the two groups have evolved live-bearing independently. However, only a minor change in the tree would be needed to join ptyctodonts and arthrodires together in a clade (that is, forming a single side branch), and thus make the offending stem segment disappear. A more important question is whether the most primitive placoderms, such as the antiarchs (bottom-feeding fishes with armoured pectoral fins), were also live-bearers, because this would undermine the case for the placoderms forming a paraphyletic segment of the gnathostome stem.

Long and colleagues<sup>1</sup> argue that the antiarchs had external fertilization. They lack pelvic fins altogether, and fossils have been found of free-living juveniles that are small and undeveloped enough to correspond to the embryos of *Materpiscis*, *Austroptyctodus* and *Incisoscutum*. It may thus be that both internal fertilization and live-bearing evolved within the placoderms. Perhaps this was a unique innovation in one placoderm clade. Alternatively, could some placoderms be stem gnathostomes and others, those with internal fertilization, stem chondrichthyans? Possibly, but this conflicts with new evidence that the acanthodians (vaguely shark-like fishes, with fin spines and tiny scales, which became extinct about 250 million years ago) form a paraphyletic array encompassing the bases of the chondrichthyan and osteichthyan lineages (Fig. 1a).

The tangled skein of jawed-vertebrate origins continues to challenge researchers. But discoveries such as the placoderm embryos of Gogo are giving us the tools to gradually untangle it — as well as showing us intimate glimpses of life in a lost world.

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with small bumps, sometimes developed into nasty, self-sharpening scissor blades. The largest of these fishes equalled the size of a great white shark and must have been formidable predators, but most were less than a metre in length.

Working with three-dimensional placoderm fossils from Gogo in Western Australia, Long and colleagues have discovered specimens of three different placoderms, *Materpiscis*<sup>2</sup>, *Austroptyctodus*<sup>2</sup> and *Incisoscutum*<sup>1</sup>, that contain minute but perfectly preserved armour plates of the same species in their body cavities. When first discovered, they were thought to be stomach contents<sup>3</sup>. But the plates show no bite marks or etching by stomach acids, and are not mixed with bones from other species; they are the remains of unborn embryos. In *Materpiscis*, a curving tubular structure associated with one of them has been interpreted as an umbilical cord<sup>2</sup>.

Embryos in the body cavity imply internal fertilization. It was noted long ago<sup>4</sup> that ptyctodonts, the placoderm subgroup to which *Materpiscis* and *Austroptyctodus* belong, have sexually dimorphic pelvic fins, somewhat like the 'claspers' used for internal fertilization in sharks. Arthrodires, the placoderm group that includes *Incisoscutum*, lack the sexually dimorphic external bones present on the pelvic fins of ptyctodonts. However, Long *et al.* argue that the partially preserved internal fin skeletons of their specimens indicate a shark-like structure, probably implying sexual dimorphism and internal fertilization. Ptyctodonts and arthrodires seem to be closely related, and so internal fertilization, and possibly live birth of young, are probably shared features retained from their common ancestor.

The living jawed vertebrates, or gnathostomes, fall into two groups, the Chondrichthyes and the Osteichthyes (Fig. 1). The Chondrichthyes (sharks, rays and ratfishes) all have internal fertilization, and many give birth to live young, whereas the ancestral condition for the Osteichthyes (ray-finned fishes, lobe-finned fishes and land vertebrates) is to spawn small eggs that are fertilized externally. Live-bearers tend to produce much fewer young than external spawners and have lower potential rates of population growth. This contrast in reproduction puts a new perspective on the ecology of the Gogo environment, a tropical reef<sup>5</sup>, where a wide diversity of placoderms coexisted with lungfishes and primitive ray-finned fishes that were probably externally fertilizing spawners. It is also interesting to note that the extinction of the placoderms at the end of the Devonian was followed by a major diversification of chondrichthyans. But it is to the study of gnathostome interrelationships that the discoveries of Long *et al.* may prove to be most pertinent.

Ideas about the origin of gnathostomes are currently in a state of flux. For much of the twentieth century, placoderms were regarded as relatives or possibly ancestors of chondrichthyans<sup>4</sup>, partly because they seemed to use internal fertilization. But recently the majority view has placed them in the gnathostome stem group<sup>6</sup> — that is, the common ancestral lineage of the living jawed vertebrates. A new analysis by Brazeau<sup>7</sup> suggests that placoderms may not be a natural group at all, but a 'paraphyletic array' spread out along the gnathostome stem (Fig. 1a; contrast with Fig. 1b). If that is correct, placoderms become extremely informative about the origin of