which it is being inserted, which takes up valuable space in the therapeutic agent. And third, the generation of a DSB has an associated risk<sup>11</sup>, albeit a manageable one. Both Peters *et al.*<sup>6</sup> and Klompe *et al.* suggest that the reported transposons provide, in principle, a solution to all those issues: the transposon integration process does not require a DSB at the target (Fig. 1b), or flanking DNA in the therapeutic agent, and should work in nondividing cells. Hence, it could be an attractive approach for human gene editing in the clinic.

However, a long checklist must be completed before clinical applications can be considered seriously. This list includes: showing that the process works efficiently at target genome positions in disease-relevant human cells (rather than in bacteria); demonstrating that it can integrate DNA fragments large enough to be clinically useful; proving its specificity in the human genome, which is about 1,000 times larger than a bacterial one; and developing ways to deliver the full complement of proteins associated with the integration process to cells without triggering the human immune response. This is a formidable workload, but a key lesson of the past 30 years of research into gene therapy is that most challenges of this type are eventually solved<sup>7,11,12</sup>. Therefore, a CRISPR system used by transposons to propagate themselves might well find itself repurposed for genetic medicine. ■

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- 1. Klompe, S. E., Vo, P. L. H., Halpin-Healy, T. S. & Sternberg, S. H. *Nature* **571**, 219–225 (2019).
- Peters, J. E., Fricker, A. D., Kapili, B. J. & Petassi, M. T. Mol. Microbiol. **93**, 1084–1092 (2014).
- 3. Barrangou, R. & Horvath, P. *Nature Microbiol.* 2, 17092 (2017).
- Jinek, M. et al. Science 337, 816–821 (2012).
  Jiang, F. & Doudna, J. A. Annu. Rev. Biophys. 46, 505–529 (2017).
- Peters, J. E., Makarova, K. S., Shmakov, S. & Koonin, E. V. Proc. Natl Acad. Sci. USA 114, E7358–E7366 (2017).
- Anguela, X. M. & High, K. A. Annu. Rev. Med. 70, 273–288 (2019).
- 8. Carroll, D. Annu. Rev. Biochem. 83, 409-439 (2014).
- 9. Urnov, F. D. CRISPR J. 1, 34–46 (2018).
- 10.Moehle, E. A. *et al. Proc. Natl Acad. Sci. USA* **104**, 3055–3060 (2007).
- 11.Porteus, M. H. N. Engl. J. Med. **380**, 947–959 (2019).

12. Dunbar, C. E. et al. Science 359, eaan4672 (2018).

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#### EVOLUTION

# Fishing out a feeding paradox

If an animal's body shape is specialized in a way that aids feeding on specific organisms, does this restrict what the animal can prey on? An observation of fishes feeding in the wild might now help to settle this question.

#### SEBASTIAN KRUPPERT & ADAM P. SUMMERS

A chance observation of fish behaviour, made during an underwater survey along the eastern shore of Lake Tanganyika in Tanzania, has now been reported in *American Naturalist* by Golcher-Benavides and Wagner<sup>1</sup>. Their observation neatly ties together 40-year-old laboratory data<sup>2</sup> and a model of evolution based on an idea known as optimal-foraging theory<sup>3</sup>.

The serendipitous event occurred when Golcher-Benavides was on a dive with a Tanzanian colleague, George Kazumbe, studying the species present in a region perpendicular to the lake's shoreline. They saw ahead, sparkling between the lake's surface and its rocky bottom, a massive school of juvenile sardines, estimated to comprise at least 50,000 individuals. Video footage of this event captured what happened when the sardines encountered fishes belonging to a group called the cichlids. There are about 250 species of cichlid fish in Lake Tanganyika<sup>4</sup>. These species represent fishes that have a wide variety of feeding specializations, including those that have evolved in a way that allows them to target a single type of prey<sup>5-7</sup>, as well as fishes that are capable of eating diverse sources of food. The shapes and features of the heads of some cichlid species bear witness to the adaptation that is suited to their particular food source (Fig. 1).

One example of a cichlid species that has evolved a feeding specialization is *Perissodus microlepis*. This fish has a curved head, and when it swims alongside a larger fish, it can suddenly attack and snatch a mouthful of scales<sup>8</sup>. The population of this species is split between fish whose head is curved to the left for attacking the right side of its fish prey, and fish whose head is bent rightward to enable an assault on the prey's left side. Other cichlid feeding specializations include those for scraping algae from rocks<sup>9</sup>, biting out the eyes of other fish<sup>10</sup>, and gobbling eggs knocked out



## 50 Years Ago

Assisted by off-stage noises which included a belching elephant seal, a giant toad in mating cry ... and the song of a wren played at slow speed, the British Library of Wildlife Sounds (BLOWS) was opened recently by Mr David Attenborough ... The library ... aims to be the national reference collection of wildlife sounds of all descriptions ... Used in conjunction with other biological reference collections, BLOWS should have an important part to play in research into animal behaviour, taxonomy and evolution ... The library's target is 10,000 recordings (disk or tape) of 2,500 species of animal in five years, and Mr Attenborough appealed for copies of commercial gramophone records ... and for copies of properly documented tape recordings of any animal sound made by either professional or amateur tape recordists.

From Nature 12 July 1969

## **100 Years Ago**

In the April issue of the Journal of Mental Science ... Capt. O. P. Napier Pearn describes the differences and similarities in the actual insanities (psychoses) found in military and civil practice ... He has collected and tabulated the facts relating to 200 cases which made a sufficiently good recovery to warrant their being returned to duty ... [W]hile at the onset of a mental disorder in civil life the friends and relatives usually co-operate with the sick person in shielding him from medical advice, such a patient in the Army ... is much more likely to receive attention from his medical officer at an early stage. The effect of this early care is that these cases respond to treatment in a very gratifying way ... The article, while laying claim to no new discovery, lays additional emphasis upon the urgency of the early treatment of mental disorders. From Nature 10 July 1919



**Figure 1** | **Cichlid fishes.** Some species of fish belonging to a group called the cichlids have body-shape specializations that help to capture specific types of prey. For example, *Petrochromis polyodon* (**a**) has large lips, which enable this species to scrape algae from rocks, whereas *Haplotaxodon microlepis* (**b**) has an upward-oriented mouth that is suited to feeding on zooplankton floating in the water. It has been debated whether cichlid feeding specialists eat only the

food that they have evolved to target. If specialists can still target a variety of food sources, this poses the condundrum, termed Liem's paradox, of how such specializations evolve. Golcher-Benavides and Wagner<sup>1</sup> report an observation of wild cichlids, including the species shown, that encountered a school of sardines they are not specialized to feed on. *P. polyodon* did not eat the sardines; however, *H. microlepis* switched from its usual food source to eat the sardines.

of the mouths of brooding parents<sup>11</sup>.

It was thought that these feeding specializations allowed specific food sources to be targeted as a way of handling intense competition for food. However, during the late 1970s and early 1980s, the biologist Karel Liem made some muscle recordings of cichlids during prey capture in the laboratory<sup>2</sup>. These showed that some specialized cichlids retain the capacity to make the movements necessary to capture a range of prey. Liem therefore asserted that it was a paradox (now referred to as Liem's paradox) that a fish best suited to a single type of prey could be a jack-of-all-trades.

But if specializing carries no penalty in terms of limiting the type of food a fish can eat, there should be little competition-driven need for specialization. Liem's paradox was met with scepticism, because it seemed to contradict a basic principle of evolution: ecologists view competition for food as a key driver of evolutionary processes of selection.

To try to resolve this debate, evolutionary biologists Beren Robinson and David Wilson developed a mathematical model<sup>3</sup> describing how feeding specialization might offer a competitive advantage. Their modelling suggested that rare periods of food scarcity could drive the evolution of a body form that has a specialized feeding capacity, while leaving intact the ability to eat other commonly available, easy prey. This hypothesis, based on optimalforaging theory, shows how competition could still have a role in explaining Liem's paradox. It made a distinction between versatility and specialization - even though a certain head shape evolved during natural selection to target a specific type of prey, this head shape might still function well to capture a wide range of easy prey.

Robinson and Wilson's theoretical framework provided a crucial insight into

Liem's paradox, and it is consistent with evidence indicating that the diets of fishes that differ in their form can still broadly overlap<sup>12</sup>. However, there is an asymmetry in the tradeoffs between food handling and competitiveness: gaining the capacity to target a low-payoff dietary item might cost little in terms of eating high-payoff, easy prey, but if such a change resulted in loss of the ability to eat easy prey, it would be expensive for the predator. The fingerprints of evolutionary selection on the shape of a fish's head should reflect the need to acquire the rare food items that get a species through adverse times, not items that represent food staples or windfalls.

How well do these theories reflect what happens in the wild? Only limited results have been reported so far. For example, there is evidence that the diets of two cichlid species of algal scrapers include more than just algae<sup>13</sup>. Golcher-Benavides and Wagner's report now provides comprehensive evidence of what happens when specialists encounter easy and abundant prey, in the form of sardines, that they are not specialized to eat. The researchers estimated that around 870 cichlids from 31 species fed on the sardines. The cichlids had abandoned the prey on which they are specialized to feed in favour of these easy pickings. Some of the cichlids that the authors observed - which might normally eat only fish scales or eyes, or the biofilms (made of organisms such as bacteria and algae) that collect on submerged rocks - feasted on sardines by reverting to their juvenile, suction-based mode of feeding.

The cichlids identified in the encounter with the sardines fell into ten groups, corresponding to their typical mode of specialist feeding. Fishes from eight of the groups enthusiastically attacked the sardines, but cichlids in two groups seemed to have made too great a trade-off in specialization and missed out on the feast. In particular, cichlids that had a strongly downward-facing mouth or 'tricuspid', alga-combing teeth didn't take the sardine snack.

This single observation gives field-based support for a theory that sprang from experimental observations. It also demonstrates the importance of the well-trained and mentally prepared naturalist who can fit real-world observations into a framework that encompasses the scientific literature and personal experience.

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- 1. Golcher-Benavides, J. & Wagner, C. E. Am. Nat. https://doi.org/10.1086/704169 (2019).
- Liem, K. F. Integr. Comp. Biol. 20, 295–314 (1980).
  Robinson, B. W. & Wilson, D. S. Am. Nat. 151, 223–235 (1998).
- 4. Brawand, D. et al. Nature **513**, 375–381 (2015).
- Clabaut, C., Bunje, P. M. E., Salzburger, W. & Meyer, A. *Evolution* **61**, 560–578 (2007).
   Chakrabarty, P. & Douglas, M. E. *Copeia* **2005**,
- onandourly, 1: & Douglas, M. E. Copela 2003, 359–373 (2005).
   Motta, P. J., Clifton, K. B., Hernandez, P. &
- Motta, F. J., Gillotti, K. B., Hernandez, F. & Eggold, B. T. *Environ. Biol. Fishes* 44, 37–60 (1995).
- Takahashi, R., Moriwaki, T. & Hori, M. J. Fish Biol. 70, 1458–1469 (2007).
- 9. Yamaoka, K. Àfr. Study Monogr. **4**, 77–89 (1983). 10.Fryer, G. & Iles, T. D. The Cichlid Fishes of the Great
- Lakes of Africa: Their Biology and Evolution (TFH, 1972).
- 11.McKaye, K. R. & Kocher, T. *Anim. Behav.* **31**, 206–210 (1983).
- 12.Boyle, K. S. & Horn, M. H. *Mar. Ecol. Prog. Ser.* **319**, 65–84 (2006).
- 13.McKaye, K. R. & Marsh, A. *Oecologia* **56**, 245–248 (1983).

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