

## Highlight: Big Surprises from the World's Smallest Fish

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In the murky blackwaters of the peat swamp forests of Southeast Asia lives the world's smallest fish, the dwarf minnow of the genus *Paedocypris*. This extreme environment, characterized by low oxygen and high acidity, is home to several miniaturized fish species. *Paedocypris* adults are a mere 8–12 mm in length and resemble zebrafish larvae, a phenomenon known as progenesis. In the case of *Paedocypris*, this developmental truncation is extreme, with over 40 bones found in zebrafish adults that never develop at all in *Paedocypris*.

It was not long after the discovery of *Paedocypris* (Kottelat et al. 2006) that Ralf Britz from the Natural History Museum in London and his collaborator Lukas Rüber from the Natural History Museum in Bern determined to learn more about these tiny vertebrates and the molecular basis of their developmental truncation. Initial studies of *Paedocypris* genes indicated that something was, well, fishy about them, as the taxonomic position of *Paedocypris* was difficult to pin down based on gene sequence data.

Now, over a decade after the discovery of these miniature fish, Britz and Rüber have finally gotten their wish. In a recent article published in *Genome Biology and Evolution* (Malmstrøm et al. 2018), Rüber and Britz, along with lead author Martin Malmstrøm of the University of Oslo, as well as a team of international collaborators including Heok Hui Tan in Singapore, Norsham Yaakob in Malaysia, and Renny Hadiaty in Indonesia, present the genome sequences of two *Paedocypris* species. As expected, following the results of their earlier genetic research, the genomes of these small fish held some big surprises.

Like the fish itself, the genome of *Paedocypris* is tiny. The *Paedocypris* genome is about one-third that found in zebrafish, a closely related model fish species. For Walter Salzburger, another coauthor of the study, this apparent pattern of reduction is the most exciting finding from their study of *Paedocypris*, as it indicates that “the extreme reduction seen in their adult phenotype is also manifested at the level of their genomes.” The authors note, however, that it is currently unclear how these two features—genome size and

body size—are related. As they explain, it may be that the extreme environment in which these fish live imposes resource limitations that may favor both a smaller genome size and a progenetic phenotype.

While the shrinking of the genome in *Paedocypris* mostly involved the loss of intronic and repetitive sequences, rather than the loss of a large number of genes, Malmstrøm et al. identified some gene losses that were quite surprising. *Paedocypris* appears to have lost dozens of key developmental genes including, most notably, at least seven and possibly as many as ten *Hox* genes. *Hox* genes encode highly conserved transcription factors that are generally considered essential for head-to-tail body patterning during early development in all animals. “The most surprising result from this study is, without a doubt, the fact that these tiny fishes have lost so many of the otherwise highly conserved vertebrate *Hox* genes,” says Malmstrøm, an opinion that is shared by Rüber and Britz. Referring to the fact that a full 15–20% of zebrafish *Hox* genes are absent in *Paedocypris*, Malmstrøm continues, “We knew from previous anatomical work that *Paedocypris* were spectacular in many ways, and we did expect some loss of genes involved in various developmental pathways, but this unprecedented loss of *Hox* genes shocked even us.”

According to William A. Cresko from the University of Oregon, who has observed *Hox* gene losses in the distantly related Gulf pipefish (Small et al. 2016), which has lost the ability to form ribs, this new work on *Paedocypris* not only “completes several genome projects in other highly derived fish species” but also begins to answer deeper questions about the nature of the evolutionary processes that lead to changes in developmental programs. “A key advance in evolution of development (evo-devo) studies in the late 20th century was finding deeply conserved developmental genetic programs in multicellular organisms, including *Hox* gene clusters in animals. In my mind, this has led to the defining evo-devo question now, which is, where in the context of deeply conserved developmental genetic programs does the genetic variation that contributes to highly divergent and novel traits reside?”

In order to answer such questions, the international team plan to continue their study of *Paedocypris* and of other miniaturized species living in the same habitat. One concern for all of the authors is, however, the potential for the loss of their unique study subjects. Says Rüber, “Doing fieldwork in poorly sampled areas often feels like a race against time, as the destruction of habitats even in remote parts of our world is happening at an ever increasing speed. Especially in the case of *Paedocypris*, several peat swamp forest habitats where these amazing fishes were collected during the first decade of the 21st century. . .have now completely disappeared, as the water has been drained, the forest cut down, and oil palm plantations have taken their place.” Unfortunately, such

habitat destruction currently threatens many valuable biological resources, including the world's smallest fish.

### Literature Cited

- Kottelat M, Britz R, Hui TH, Witte K-E. 2006. *Paedocypris*, a new genus of Southeast Asian cyprinid fish with a remarkable sexual dimorphism, comprises the world's smallest vertebrate. *Proc Biol Sci.* 273(1589):895–899.
- Malmstrøm M, et al. 2018. The most developmentally truncated fishes show extensive *Hox* gene loss and miniaturized genomes. *Genome Biol Evol.* Available at: <https://doi.org/10.1093/gbe/evy058>.
- Small CM, et al. 2016. The genome of the Gulf pipefish enables understanding of evolutionary innovations. *Genome Biol.* 17(1):258.

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