

How the African clawed frog got an extra pair of genes

Whole genome sequence reveals evolutionary history of *Xenopus laevis*

The African clawed frog's ancestor inherited one set of chromosomes each from two different species and doubled its whole genome some 18 million years ago, according to an international research consortium led by Japanese and American scientists who sequenced the entire genome of the *Xenopus laevis* for the first time. Scientists hope that the finding will help our understanding of vertebrate evolution, as the vertebrate genome doubled twice 500 million years ago.

X. laevis is unusual in that it is a tetraploid species that has four sets of chromosomes, while many organisms, including humans, are diploid and have two sets of chromosomes. How and when this came about has been a topic of debate for some time.

One hypothesis is that the tetraploid *X. laevis* inherited one half of its genetic material from each parent when two diploid ancestral species mated, and the genome of this diploid offspring then doubled, giving rise to a tetraploid organism with twice the number of chromosomes as its ancestors.

X. laevis is an essential organism for biological and biomedical research, but the sheer size and complexity of its genome made it difficult for scientists to sequence the genome in its entirety. Sequencing the entire genome would not only be valuable for biological and biomedical research but also provide clues as to the origins of tetraploidy.

The researchers sequenced the entire genome of the J (Japan) strain of the frog inbred in Japan, in which the genetic codes inherited from the mother and father, respectively, are identical.

The US team led by Dan Rokhsar and Richard Harland at the University of California, Berkeley, used the shotgun method to sequence short fragments of DNA and piece them together like a puzzle. The Japanese team led by Masanori Taira at the University of Tokyo sequenced very long fragments of DNA and determined the location of the long DNA on the chromosomes. This extra step helped to distinguish the separate genome sequences inherited from each ancestral species.

It was a challenging idea to analyze the 'transposable elements' (segments of DNA that move around the genome) that become fixed or inactive over time, but might be one way of tracing the two ancestral genomes, present as subgenomes in *X. laevis*. Akira Hikosaka at Hiroshima University and Yoshinobu Uno at Nagoya University tested this idea and discovered that indeed two sets of chromosomes originated from different diploid ancestors.

Curiously, the scientists also found that the subgenomes evolved separately in the nucleus, giving rise to shorter S and longer L types, the first evidence of animal subgenome evolution. The L type chromosomes preserved most of the ancestral genetic information, while the S type showed greater gene loss, deletion and rearrangement.

Scientists believe that two rounds of whole genome duplication 500 million years ago contributed to the emergence of the first vertebrate species and an explosion of diversity in this group. The new findings from the *X. laevis* genome should improve our understanding of this important event in our evolutionary history.



Figure 1: African clawed frog (right) and Western clawed frog
 Caption: Though similar in appearance, the tetraploid *Xenopus laevis* adult female is noticeably larger than its counterpart in the related diploid species *Xenopus tropicalis*.
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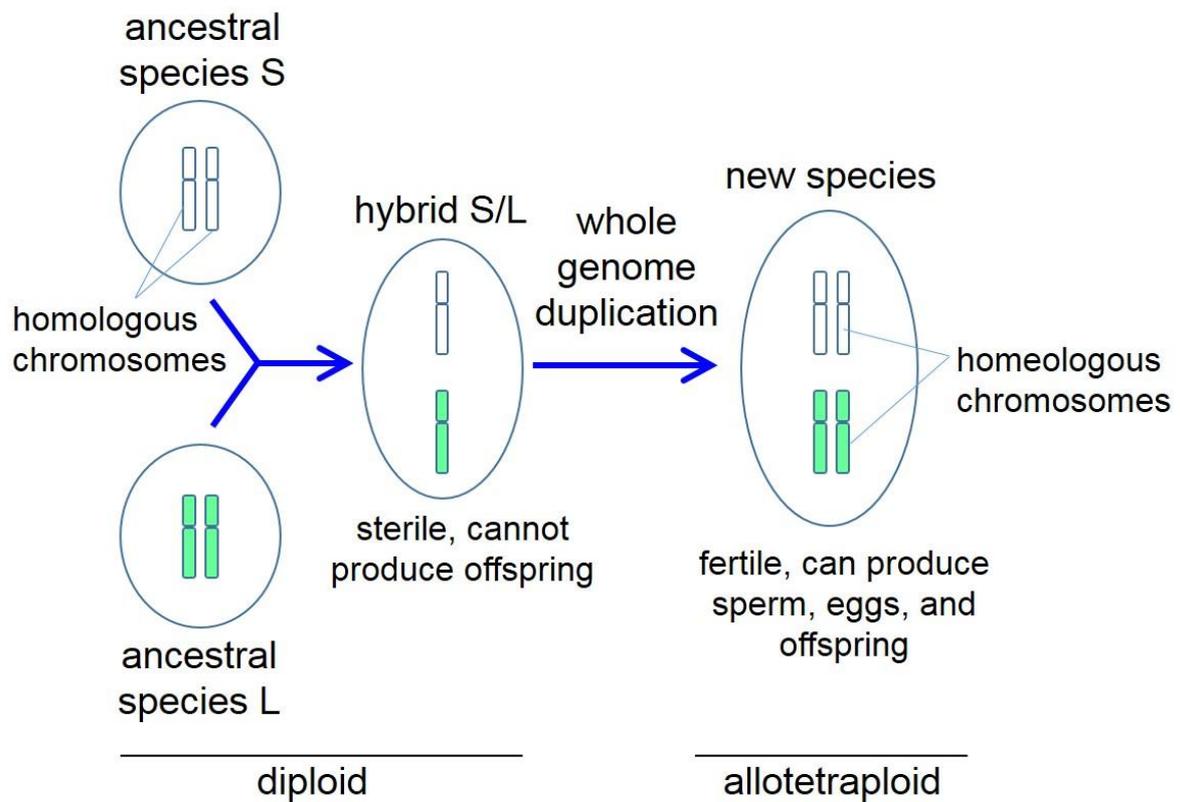


Figure 2: Genesis of the *Xenopus* ancestor
 Caption: Two ancestral species with nine pairs of chromosomes, S and L, mate to produce a hybrid S/L offspring with 18 chromosomes that do not pair. This sterile offspring undergoes

whole genome duplication to produce a new fertile species with 18 pairs of chromosomes that is ancestral to all *Xenopus* species. For clarity, the process is rendered here with only one type of chromosome.

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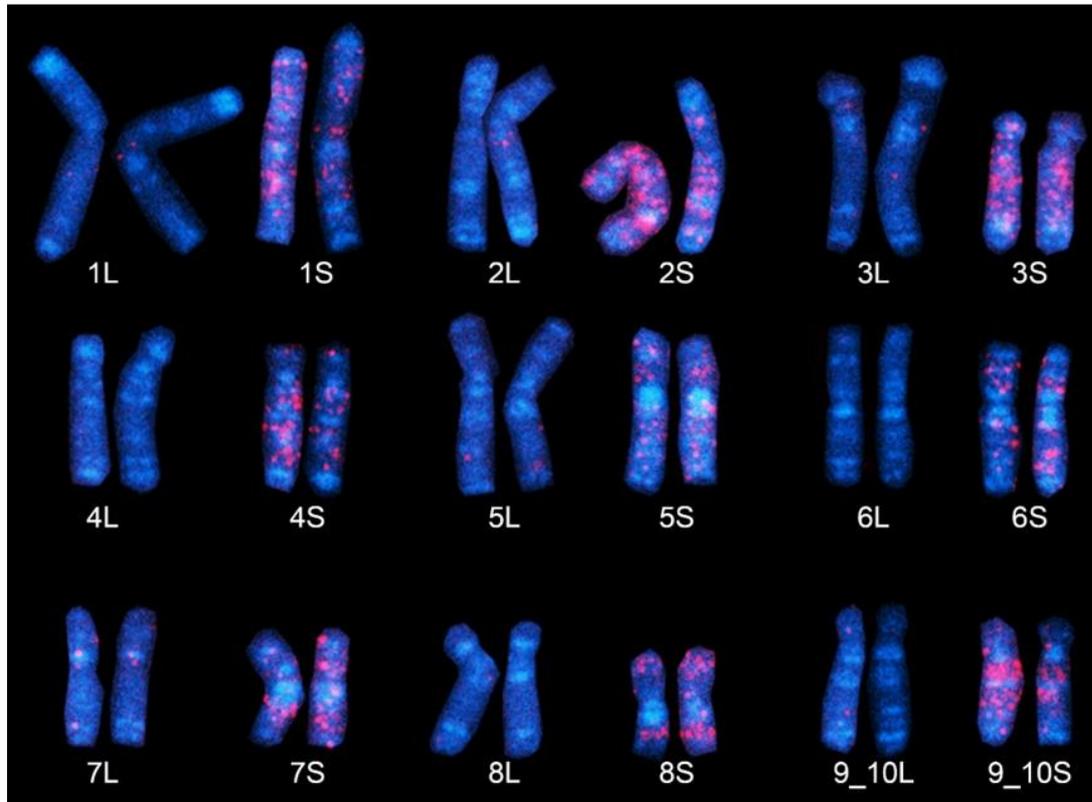


Figure 3: African clawed frog chromosomes

Caption: “Fossil” DNA sequences found only in the S subgenome (chromosomes) of *Xenopus laevis* emit a red glow employing the FISH method. The nine S chromosomes here clearly possess a larger number of red regions, believed to have derived from ancestral species S. (Chromosome 9, at bottom right, is represented as “9_10,” as it corresponds to the fusion of ancestral chromosomes corresponding to chromosomes 9 and 10 in *Xenopus tropicalis*).

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Collaborating institutions

(Japanese team, 30 out of 74 researchers from the following institutions were involved)

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Nagoya University

Hiroshima University

National Institute for Basic Biology

National Institute of Advanced Industrial Science and Technology

Hokkaido University
Nagahama Institute of Bio-Science and Technology
Yamagata University
National Center for Child Health and Development
Tokyo Institute of Technology
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