

specialization of the snail's brain that has been attributed to the appearance of the retractable nose. As Van Mol² was the first to point out, a prominent procerebral lobe is present in all stylommatophore species but in no basommatophore species. Could the brain of caecilians have a comparable adaptation? The possibility is suggested by numerous analogies that are evident in the olfactory systems of snails and vertebrates. Convergent features include the cellular organization of the sensory epithelium, the presence of synaptic glomeruli and the generation of oscillating field potentials^{3,4}. Given that snails and caecilians seem to be the only ani-

mals with mobile and retractable eye/nose structures, there might be curiosities to discover in the caecilian brain, especially in those regions that receive afference from the tentacle.

Ronald Chase
 Department of Biology,
 McGill University,
 1205 Ave. Docteur Penfield,
 Montreal, Quebec, H3A 1B1,
 Canada
 e-mail: rchase@bio1.lan.mcgill.ca

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Transposable element in fish

SIR — Several transposable elements of the terminal-inverted-repeat class have been described in vertebrate genomes¹. Some of them are thought to be active because of their presence in gene regions or polymorphic situations. However, demonstration of *de novo* excision or insertion of such elements has hitherto not been described to our knowledge. We have identified a novel terminal-inverted-repeat class transposable element in the medaka fish *Oryzias latipes*, and have detected its excision during embryogenesis.

The *i' / i'* medaka fish genotype is associated with a complete albino phenotype², as the *i* allele is a defective tyrosinase gene³. We isolated another allele at the same locus, *i'*, from a commercial breed-

ing population: *i'* / *i'* fish have a quasi-albino phenotype. The *i'* allele is recessive to the wild-type allele *i*⁺. A description of *i'* and *i'* is available on the World-Wide Web at the *Medakafish* home page (<http://bio1.bio.nagoya-u.ac.jp:8000/>). Cloning and sequencing of the tyrosinase gene region of an *i'* / *i'* fish reveals that the fifth exon contains a 4.7-kilobase (kb) DNA insertion. We believe that the insertion sequence (*a* in the figure) is a terminal-inverted-repeat transposable element because: (1) it has inverted repeats at its termini; (2) there is duplication of a segment of the host chromosome; and (3) it is present as multiple copies. We have called this transposable element *Tol2*, and the particular copy found in the tyrosinase gene *Tol2-tyr*.

About 10 copies are present in the diploid genome.

Tol2 contains 4 open reading frames with amino-acid sequence similarity to *Ac* of maize⁴, *hobo* of *Drosophila*⁵ and *Tam3* of *snapdragon*⁶ (see Supplementary Information at *Nature's* website, <http://www.nature.com>). We propose that these elements have diverged from a single ancestor⁷.

Transposable elements of the terminal-inverted-repeat class are thought to move in a cut-and-paste fashion. To detect excision of *Tol2* during embryogenesis, we conducted polymerase chain reaction (PCR) using a pair of primers which encompass *Tol2-tyr* and are 0.5-kb apart on the wild-type tyrosinase gene⁸. We used genomic DNAs of 5-day-old albino embryos as templates. We examined 60 embryos individually, and all show 5.2-kb

products. In addition, we observed 0.5-kb fragments from 8 of the 60 embryos examined (see Supplementary Information). We cloned and sequenced these 0.5-kb fragments and grouped the sequences obtained into six types, all featuring total, or near-total, loss of the *Tol2-tyr* sequence (*b* in the figure). Type 5 is identical to the wild-type fish product. In the other five types, some nucleotides of the target site duplication or a *Tol2* terminal region are retained. Thus our PCR analysis provides evidence for *de novo* excision of *Tol2*, with good but not absolute precision. Excision with some nucleotides left behind has also been observed for *Ac*⁹ and other terminal-inverted-repeat class transposable elements.

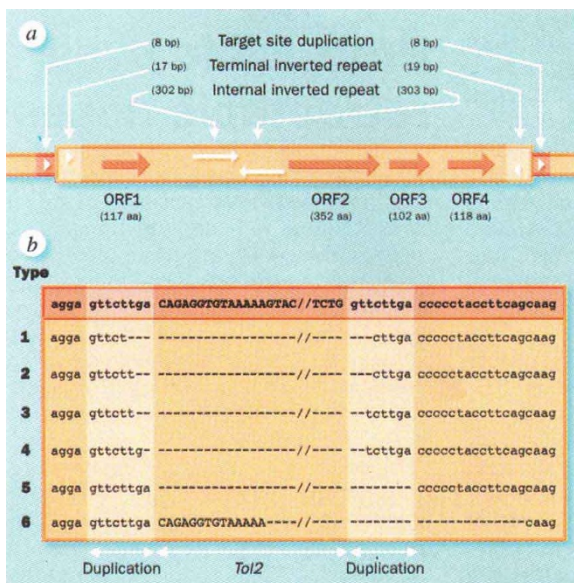
Whether *Tol2-tyr* itself is an autonomous member is not yet known. It is evident from our results, however, that an autonomous member is present somewhere in the genome. *Tol2* is thus a unique tool for establishing a gene tagging system in fish, and possibly also in other vertebrate species.

Akihiko Koga
Miho Inagaki
Hidehito Suzuki
Yoshitaka Bessho
Hiroshi Hori
 Department of Biology, Faculty of Science,
 Nagoya University, Nagoya 464-01, Japan

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Dynamics of haemoglobin

SIR — Jia *et al.* describe a possible physiological role of nitrosylated haemoglobin, postulating a dynamic cycle in which oxygenated haemoglobin in arterial blood is S-nitrosylated and the NO group is released to bind to the haem of deoxygenated haemoglobin during arterial-venous transit¹. Thus the authors predict, citing ref. 2 as an example, that haemoglobin with haem-bound NO may not be observed in arterial blood but may be in venous blood. They contend also that the anticipated normal levels of haem-nitrosylated haemoglobin *in vivo* are too low to be detected by direct measurements (for example, electron paramagnetic resonance (EPR) spectroscopy).



Characterization of *Tol2*. *a*, Structure. Total length, 4,681 bp (GenBank accession number D84375). *b*, Excision footprints. Nucleotides of *Tol2* and the tyrosinase gene are shown in upper and lower case, respectively. Dash, no nucleotide occupation. The boxed sequence is from the genomic clone of the tyrosinase gene region that contains *Tol2*.