

LABORATORY OF BIORESOURCES

Associate Professor
NARUSE, KiyoshiPostdoctoral Fellow
Technical AssistantsSHEN, Xueyan
KOIKE, Yukari
TORII, Naoko
AJIOKA, Rie
SUZUKI, Tokiko

Secretary

Teleosts comprise about half of all vertebrate species and adapt to a variety of environments, including sea-water, fresh water, the bottom of deep seas, and small creeks and paddy fields. Analysis of their genome structure is important to understand the adaptation and diversification in this interesting group. Medaka is a small egg-laying “secondary” fresh water fish found in brooks and rice paddies in Eastern Asia. This species has a long history as an experimental animal, especially in Japan. Our laboratory has conducted a comparative genomic analysis focusing mainly on fish chromosomes and gene evolution using medaka and other fishes. In addition to these activities, our laboratory is stepping ahead to lead the National BioResource Project Medaka (NBRP Medaka).

I . Medaka genome sequence and the vertebrate genome evolution

We have successfully completed the genome sequencing of Hd-rR (Southern inbred strain) at the draft level. Total nucleotide length of the generated scaffolds is 700.4Mbp. Comparative analysis with the genome of the northern inbred line (HNI) revealed 16.4 million single nucleotide polymorphisms (SNPs) which allowed us to develop a high density SNP map that could be successfully used for

aligning generated scaffolds. The genome-wide SNP rate between Hd-rR and HNI inbred strains is 3.42 % which is, to our knowledge, the highest SNP rate seen in any vertebrate species. We also identified 20,141 non-redundant genes with 5'-end serial analysis of gene expression (SAGE) tags combining with Genscan. Using this medaka gene model, we conducted four-way comparisons of the synteny of orthologous genes among the human and *Tetraodon* genomes and the zebrafish gene map. Most of the medaka and *Tetraodon* chromosomes have a one-by-one relationship and about half of the medaka and zebrafish chromosomes also correspond to a one-by-one relationship, even though the lineage separation of these two species dates back more than 191 million years. These results showed that the inter-chromosomal arrangements in the teleost lineage were less frequent than those of mammals whose lineage separation dates back to 100 million years ago. We also successfully reconstructed the pre-duplicated proto-chromosomes of the ancestor of all ray-finned fish and described the scenario leading to the present genome structure of medaka, zebrafish and *Tetraodon*.

II . Evolution of the sex chromosome and sex determination genes in *Oryzias* fish

The sex-determining gene *DMY* was identified on the Y chromosome in the medaka, *Oryzias latipes*. However, this gene is absent in most *Oryzias* fishes, suggesting that closely related species have another sex-determining gene. In fact, it has been demonstrated that the Y chromosome in *O. dancena* differs from that in *O. latipes*, whereas both species have an XX/XY sex determination system. Through a progeny test of sex-reversed fish and a linkage analysis of isolated sex-linked DNA markers, we showed that *O. hubbsi*, which is one of the species most closely related to *O. dancena*, has a ZZ/ZW system.

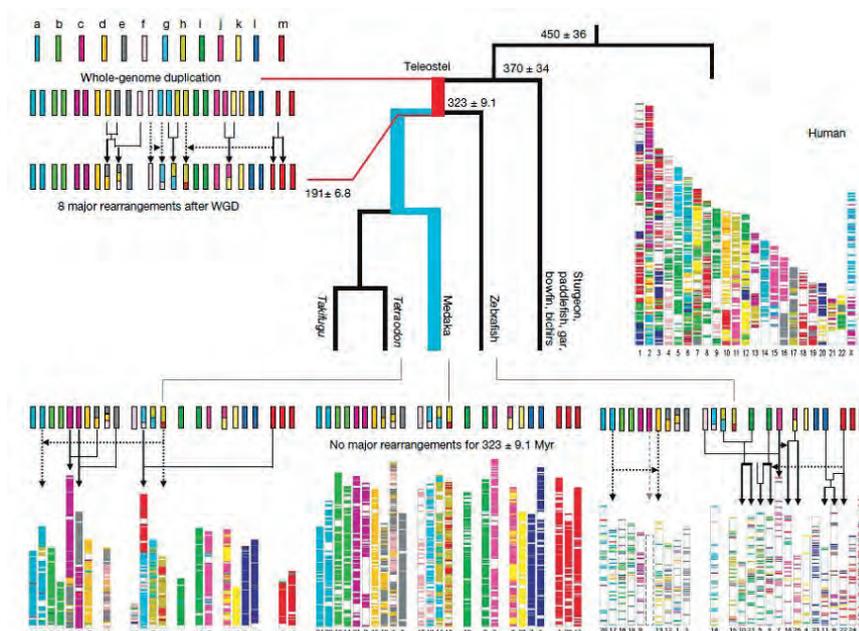


Figure 1. Reconstruction of the pre-duplicated proto-chromosome and scenario leading to the medaka, *Tetraodon* and zebrafish genome

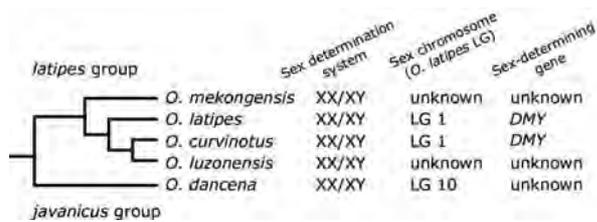


Figure 2. Phylogenetic relationships and sex determination mechanisms in *Oryzias* fishes

III. National BioResource Project Medaka (NBRP Medaka)

In 2007, the NIBB was selected as the core facility of NBRP medaka. Our laboratory is taking an active part of this project. We provide, maintain and collect living resources such as standard strains, inbred strains, mutants, and frozen resources such as EST/cDNA and BAC/ Fosmid clones, as well as the integrated information on medaka with the goal of facilitating and enhancing the use of medaka as a model organism. NBRP Medaka is aiming to establish a first rate biological resource with the highest possible levels of accessibility and ease of use.

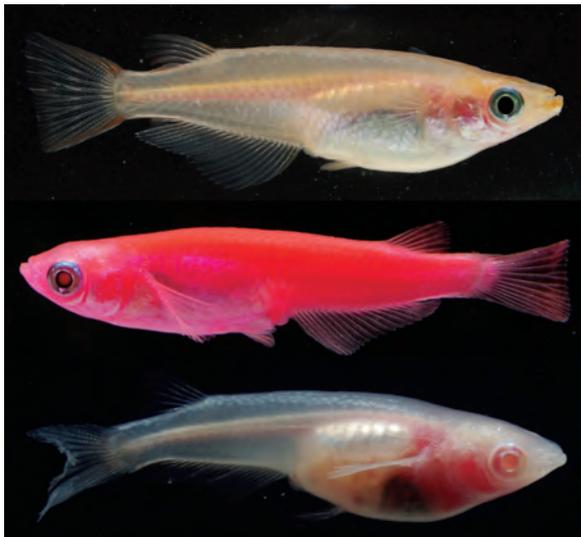


Figure 3. Medaka provided from NBRP Medaka

Publication List

[Original papers]

- Hojo, M., Takashima, S., Kobayashi, D., Sumeragi, A., Shimada, A., Tsukahara, T., Yokoi, H., Narita, T., Jindo, T., Kage, T., *et al.* (2007). Right-elevated expression of charon is regulated by fluid flow in medaka Kupffer's vesicle. *Develop. Growth Differ.* 49, 395-405.
- Kasahara, M., Naruse, K., Sasaki, S., Nakatani, Y., Qu, W., Ahsan, B., Yamada, T., Nagayasu, Y., Doi, K., Kasai, Y., *et al.* (2007). The medaka draft genome and insights into vertebrate genome evolution. *Nature* 447, 714-719.
- Kawaguchi, M., Yasumasu, S., Hiroi, J., Naruse, K., Suzuki, T., and Iuchi, I. (2007). Analysis of the exon-intron structures of fish, amphibian, bird and mammalian hatching enzyme genes, with special reference to the intron loss evolution of hatching enzyme genes in Teleostei. *Gene* 392, 77-88.
- Takashima, S., Shimada, A., Kobayashi, D., Yokoi, H., Narita, T., Jindo, T., Kage, T., Kitagawa, T., Kimura, T., Sekimizu, K., *et al.* (2007). Phenotypic analysis of a novel chordin mutant in medaka. *Dev. Dyn.* 236, 2298-2310.
- Takehana, Y., Demiyah, D., Naruse, K., Hamaguchi, S., and Sakaizumi, M. (2007). Evolution of different Y chromosomes in two medaka species, *Oryzias dancena* and *O. latipes*. *Genetics* 175, 1335-1340.
- Takehana, Y., Naruse, K., Hamaguchi, S., and Sakaizumi, M. (2007). Evolution of ZZ/ZW and XX/XY sex-determination systems in the closely related medaka species, *Oryzias hubbsi* and *O. dancena*. *Chromosoma* 116, 463-470.
- Tanaka, K., Takehana, Y., Naruse, K., Hamaguchi, S., and Sakaizumi, M. (2007). Evidence for different origins of sex chromosomes in closely related *Oryzias* fishes: substitution of the master sex-determining gene. *Genetics* 177, 2075-2081.
- Yokoi, H., Shimada, A., Carl, M., Takashima, S., Kobayashi, D., Narita, T., Jindo, T., Kimura, T., Kitagawa, T., Kage, T., *et al.* (2007). Mutant analyses reveal different functions of *fgfr1* in medaka and zebrafish despite conserved ligand-receptor relationships. *Develop.* Biol. 304, 326-337.