Genetic visualization and control of the neuronal activity in the zebrafish brain

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Zebrafish is an excellent model vertebrate because of high fecundity, rapid embryonic development, transparency at the embryonic stages and inexpensive and easy breeding procedures. For the past decade, we have developed genetic methods including transgensis, gene trapping, enhancer trapping and the Gal4FF-UAS system in zebrafish by using the *Tol2* transposable element. By employing these methods, we have performed a large-scale genetic screen, and generated more than 1,000 transgenic lines that expressed the yeast transcription activator Gal4 in specific cells, tissues, and organs. Gal4 can activate transcription of a gene placed downstream of its binding sequence UAS. Therefore by crossing the Gal4 transgenic fish with UAS reporter fish, the Gal4-expressing cells are visualized, and, further, by crossing them with UAS effector fish, the functions of Gal4-expressing cells can be manipulated via targeted expression of the effector genes. To make the best use of them, we constructed a web-based database named zTrap (http://kawakami.lab.nig.ac.jp/ztrap/), by which researchers can search transgenic fish of their interests based on expression patterns and genomic loci. I will introduce these important genetic methods in zebrafish and how the transgenic fish resource has been used for the study of developmental biology and organogenesis.

We are interested in understanding cellular and molecular basis of animal's complex behaviors, such as learning and memory. Therefore we aim to apply the genetic methods and the transgenic resource to the study of functional neural circuits. First, we developed a system to inhibit neuronal activity by targeted expression of a neurotoxin gene via the Gal4-UAS system. We crossed transgenic that expressed Gal4 in specific regions of the brain with the UAS-neurotoxin effector fish, performed behavioral analysis, and are identifying

functional neuronal circuits that regulate emotional learning. Second, we developed a system to visualize neuronal activity in which a DNA-encoded calcium indicator GCaMP was placed downstream of UAS. By expressing GCaMP in the brain area that receives visual inputs from retina, we successfully demonstrate real-time imaging of the brain activity during perception. I will introduce these cutting-edge researches in the field of neurobiology in zebrafish and discuss how the zebrafish research can contribute to understanding function of our brain.