Fishing novel genes in zebrafish animal model

Cheol-Hee Kim

Department of Biology, Chungnam National University, Daejeon, Korea

The zebrafish (*Danio rerio*) is a vertebrate model system suitable for fishing novel genes in post-genome era. Two neural mutants isolated from the ENU-based chemical mutagenesis, were characterized and the point mutations were identified by the positional cloning method. The first mutant is *headless* : Wnt antagonists secreted by the organizer have been identified as head inducers. The severe head defects in *headless* are due to a mutation in Tcf-3, a component of the Wnt pathway. The second is *mind bomb* : Reduced lateral inhibition in mutant permits too many neural progenitors to differentiate as neurons. *mind bomb* encodes a novel gene in the Notch pathway. In addition to chemical mutagenesis, we developed a novel transgene reporter system and tried to apply its use for the insertional mutagenesis. The first mutant "ondal" from this new screen, was characterized and mapped to a gene involved in axonal myelination and human schizophrenia. The other mutants, *moguri*, *samdori*, and *hayan*-4, are being mapped and characterized. As a separate approach, we are challenging a genome-wide screen against the human unigene collection. More than 10,000 human full-length cDNAs are available from the unigene collection. After *in silico* screening for novel genes in the genome database, we microinjected individual human gene into the *in vivo* zebrafish embryos. From this phenotype-based expression cloning, we identified several novel genes and further characterized their homologues in zebrafish.