

Evolution of brain and CNS from the viewpoint of genome and gene expression profile: What happened in the evolutionary process from planarian to human?

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The evolutionary origin of the brain remains a challenging und unsolved problem in evolutionary studies. To understand when and how the structural brain emerged, we analyzed the central nervous system (CNS) of a lower invertebrate, planarian. We determined the nucleotide sequence of more than 9,000 ESTs (expressed sequence tags) from the head portion of planarians, obtaining 3,101 non-redundant EST clones. As a result of homology search, we found that 116 clones had significant similarity to the genes related to the nervous system. Here, we compared these planarian 116 EST clones with all ORFs of the complete genome sequences of human, fruit fly, nematode, showing that over 95% of these 116 nervous system-related genes were commonly shared among these organisms. Interestingly, we found that about 30% of planarian nervous system-related genes had homologous sequences in *Arabidopsis* and yeast which do not possess the nervous system. It implies that the origin of nervous system-related genes was much older than the emergence of the nervous system.

We also conducted a large-scale screening of the head part-specific genes in the planarian by constructing a cDNA microarray. Competitive hybridization of cDNAs between a head portion and the other body portion of planarian revealed 205 genes with head part-specific spikes, including essential genes in the vertebrate nervous system. The expression patterns of the top 30 genes showing the strongest spikes implicated that the planarian brain has undergone functional regionalization. We demonstrate the complex cytoarchitecture of the planarian brain, despite its simple superficiality of the morphology.

These results obtained for planarian were also compared with the gene expression patterns of other organisms. Finally, I would like to note that the present study was conducted in collaboration with Dr. Kiyokazu Agata's group at RIKEN.

Related publications:

- Mineta, K., Nakazawa, M., Cebria, F., Ikeo, K., Agata, K. and Gojobori, T. (2003). Origin and evolutionary process of the central nervous system (CNS) elucidated by comparative genomics analysis of planarian ESTs. *Proc. Natl. Acad. Sci. USA* 100:7666-7671.
- Nakazawa, M., Cebria, F., Mineta, K., Ikeo, K., Agata, K. and Gojobori, T. (2002). Search for the evolutionary origin of a brain. ; Planarian brain characterized by microarray. *Mol. Biol. Evol.* 20:784-791.
- Cebria, F., Kobayashi, C., Umesono, Y., Nakazawa, M., Mineta, K., Ikeo, K., Gojobori, T., Itoh, M., Taira, M., Alvarado, A. and Agata, K. (2002). FGFR-related gene *nou-darake* restricts brain tissues to the head region of planarians. *Nature* 419, 620-624.

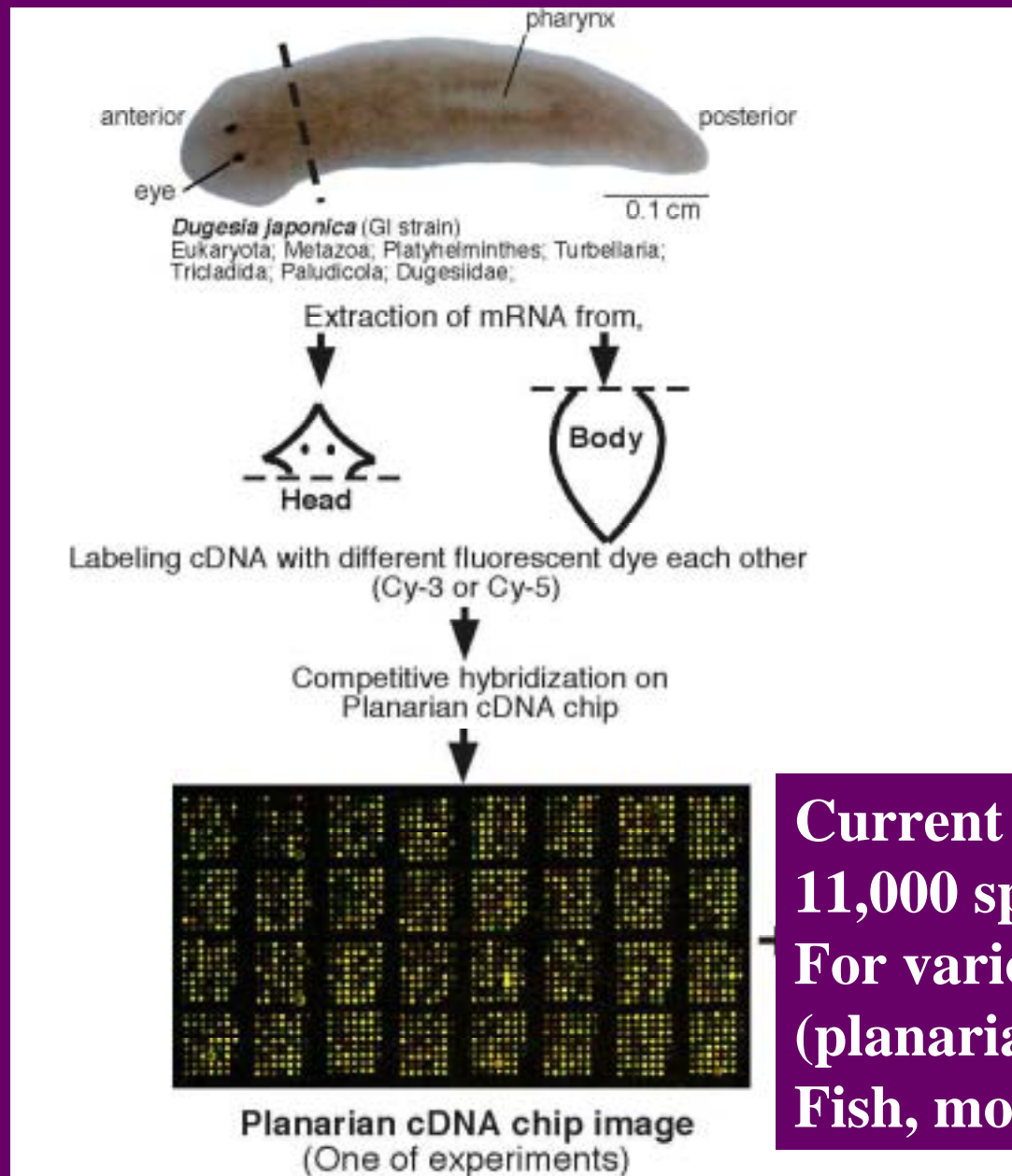


Figure 1 Flow chart demonstrating the strategy for large scale screening of planarian brain-related genes.