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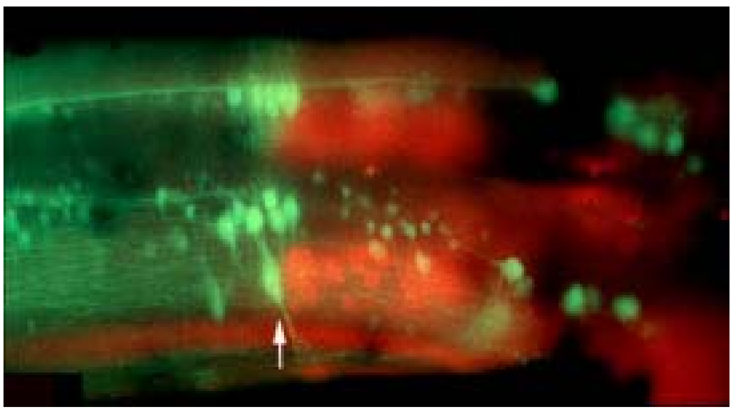
New insights into the evolution of the hindbrain

January 30, 2004 – The advent of the hindbrain is an evolutionarily important event in the organization of the central nervous system. In work published in the journal *Development*, Shigeru Kuratani and colleagues in the RIKEN CDB Laboratory for Evolutionary Morphology revealed discrete mechanisms for segmentation and neural cell specification in a one of the most primitive species known to possess a segmented hindbrain.

In vertebrates, the hindbrain is a segmented structure, subdivided into clearly demarcated units called rhombomeres, which generate specific sets of neurons. The lancelet *Amphioxus*, a more primitive chordate, however, lacks this hindbrain segmentation. The lamprey, a jawless fish that arose in the interval between non-vertebrate chordates (such as *Amphioxus*) and gnathostomes (jawed animals), provides a relevant model for studying the emergence of the hindbrain developmental plan.



Mauthner neuron (arrow), which develops in rhombomere 4 in all vertebrate species

Yasunori Murakami in the Kuratani lab labeled reticulospinal and branchial motor neurons (which derive from rhombomeres) to reveal the neuronal organization of the hindbrain of the Japanese lamprey, *Lethenteron japonicum*, and studies the expression patterns of rhombomere-specific genes. They found that lamprey reticular neurons develop in conserved rhombomere-specific positions, similar to those observed in the gnathostome zebrafish. Interestingly, in lamprey the positions of other sets of hindbrain neurons – the trigeminal and facial motor nuclei – do not map neatly to rhombomeric borderlines, as they do in gnathostomes. Rather, the trigeminal–facial nerve originates in the middle of rhombomere 4, in the region of expression of the lamprey Hox gene *LjHox3*. Murakami found that when retinoic acid (which is known to alter *Hox* gene expression and associated developmental programs) was introduced to the developing hindbrain region, it caused positional shifts of both *LjHox3* expression and branchiomotor nuclei, but no apparent changes in segmentation or the positions of reticular neurons.

These findings indicate that, in the lamprey, hindbrain neural identities and rhombomeric segmentation are governed by independent mechanisms, providing strong counter-evidence to one prevailing model that suggests that the establishment of neuronal identity is a *Hox*-dependent process. Based on their discoveries, Kuratani et al offer an alternate model in which the positional concurrence between *Hox* expression, rhombomere identity and specific subsets of hindbrain neurons is the result of a convergent process in which originally independent mechanisms became linked secondarily in the history of gnathostome evolution.

Studies such as these underscore a pair of evo-devo precepts: that molecular designs capable of supporting viable ontogenies tend to act as magnets for convergent evolution, and that Nature is parsimonious with her creations, preferring to repurpose or tinker with existing genes rather than to introduce perfect novelties.

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