CELL FATE

Space–time continuum

The ventral hindbrain of the vertebrate embryo contains a population of neuronal progenitor cells that gives rise to visceral motor neurons (vMNs) and serotonergic (5-HT) neurons. Each hindbrain segment, or rhombomere, initially generates vMNs, but all the rhombomeres except for r4 switch to producing 5-HT neurons at a defined time point (around embryonic day 10.5 in the mouse). These observations raise two crucial questions — how do progenitors switch from vMN to 5-HT neuron production, and how is r4 prevented from making this switch? In *Genes and Development*, Pattyn and colleagues show that the answers might lie with a set of homeobox genes that are also important for the spatial patterning of the hindbrain.

The *Phox2b* gene is required for the generation of vMNs in the hindbrain, and Pattyn *et al.* found that in r2–r3 and r5–r7, the switch from vMN to 5-HT neuron generation coincides with downregulation of *Phox2b* in the ventral portion of each rhombomere. In r4, on the other hand, *Phox2b* expression is maintained at all dorsoventral levels. Another feature that distinguishes r4 from the other rhombomeres is its expression of *Hoxb1*, and the authors showed that r4 can generate 5-HT neurons in *Hoxb1* mutant embryos. *Nkx6.1* and *6.2* are required to maintain *Hoxb1* expression in the ventral part of r4 — in their absence, the *Hoxb1* expression domain recedes dorsally, and r4 begins to generate 5-HT neurons at around the same time. This indicates that Hoxb1 suppresses the switch to 5-HT neuron production. Its importance was underlined in *Hoxb2* mutant embryos, where *Hoxb1* is downregulated in the ventral part of r4, but later than in the *Nkx6* mutants. In these embryos, r4 generates fewer 5-HT neurons than in the *Nkx6* mutants, implying that production of these neurons begins later, commensurate with the downregulation of *Hoxb1*.

To bring the story full circle, Pattyn *et al.* showed that Hoxb1 suppresses 5-HT neuron production by prolonging the expression of *Phox2b* in the ventral part of r4. So, the downregulation of *Phox2b* seems to be the key molecular switch that converts cells in the ventral hindbrain from vMN to 5-HT neuronal progenitors. These findings represent an important step towards understanding how the properties of neuronal progenitors in the hindbrain change over time, and future studies should uncover whether homeobox genes act to couple the spatial and temporal aspects of neuronal specification in other regions of the nervous system.

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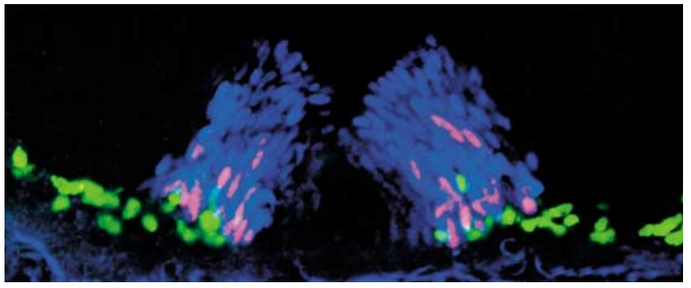

Cross section of a mouse hindbrain at embryonic day 11, just after the switch from vMN to 5-HT neuron production. The zone that gives rise to these neurons is labelled in blue. The vMNs (green) are migrating away from this zone, which is now generating 5-HT neurons (pink). Courtesy of J. Ericson, Karolinska Institute, Stockholm, Sweden.

CELLULAR NEUROPHYSIOLOGY

The rules of summation

Synaptic integration — the summation of all the inputs that a neuron receives — is a challenging problem in cellular neurobiology, owing to the unanticipated complexity of the active properties of the dendritic tree, which depend on the presence of many types of voltage-gated ion channels. One consequence of this complexity is the existence of contradictory data that point to different rules of synaptic summation. Two recent papers in *Neuron* have tried to go beyond these contradictions by proposing a new model of CA1 pyramidal neurons, which might help to clarify how integration takes place.

The model that Poirazi *et al.* propose is broader than previous examples in that it combines results from different response measures (mean versus peak amplitude of synaptic potentials), stimulus formats (single stimuli versus trains) and conditions of spatial integration (within versus between dendritic branches). Using this model, they found that, below the threshold for action potential generation, inputs sum non-linearly within higher-order branches and linearly between branches. This result has profound implications for the design of future experiments and for the interpretation of previous data.

But what about stimuli that elicit action potentials when integrated? In the second paper, Poirazi *et al.* argue that we can think about a CA1 pyramidal neuron as a two-layer 'neural network'. In the first layer, higher-order branches act as independent subunits that add inputs non-linearly. In the second layer, the dendritic trunk and the soma linearly sum the output of the subunits and compare the result to the threshold for action potential firing.

Although the model does not address other aspects of synaptic integration, such as temporal summation, and might not apply to other classes of neurons, the work of Poirazi *et al.* constitutes a useful heuristic tool that makes specific predictions, which can now begin to be empirically tested.

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