Cellular Mechanisms for the Axonal Pattern Formation: Initiation and Branch Morphogenesis

Yoshiyuki Konishi[1,2*]

[1]*Department of Human and Artificial Intelligence Systems, Graduate School of Engineering, University of Fukui, 3-9-1 Bunkyo, Fukui 910-8507, Japan*
[2]*Research and Education Program for Life Science, University of Fukui, 3-9-1 Bunkyo, Fukui 910-8507, Japan*
[*]*E-mail address: ykonishi@u-fukui.ac.jp*

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The establishment and maintenance of characteristic cellular morphology is especially important in the nervous system, in which neurons make connections with specific targets, thereby enabling the processing of information. The axonal pattern is crucial in determining the target cells, and is controlled by extracellular molecules, called axon guidance molecules. In culture, isolated neurons are capable of extending the axon and establishing mature neuronal morphology without particular cell-extrinsic cues. Molecular systems that control this cell-autonomous process remain to be elucidated. In this paper, we summarize the cellular processes of axonal patterning and some of the intracellular molecular mechanisms that contribute to maintain the axon morphology.
Key words: Neuron, Morphogenesis, Polarity, Axon, Dendrite

1. Introduction

Neurons form a highly polarized morphology by extending molecularly and functionally distinctive processes that emerge from the cell body; the axon, a single thin process that is required to transmit signals to target cells in the form of electrical impulse (action potential), and dendrites, shorter processes that receive signals. The terminal axons synapse with the dendrites of the target neurons. The presynaptic terminals of the axon release neurotransmitters to the postsynaptic site. Axonal length and morphology vary widely depending on the location of their target cells. For example, some interneurons possess only a short (a few hundred micrometers long) axon, whereas the axons of sensory or motor neurons may be over one meter long. In addition to the axon length, their branched morphology is important for information processing. Axons in the hippocampal pyramidal neurons may have hundreds of axonal branches to innervate multiple target cells. Furthermore, the axonal branch pattern of each neuron can change during development. As described in the next section, axonal pattern formation can be divided into several cellular processes.

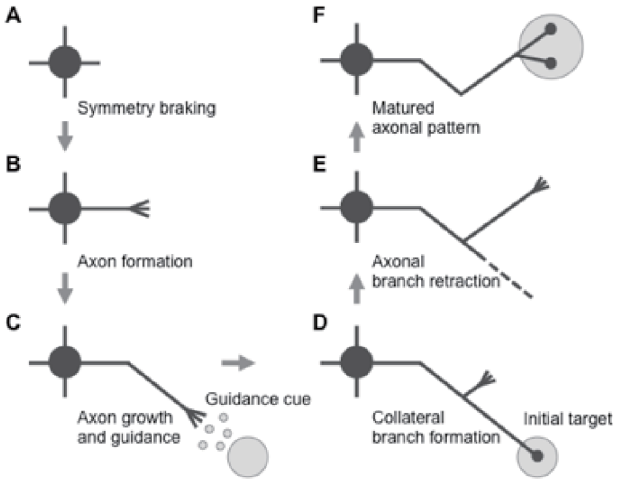

Fig. 1. The processes of axonal morphogenesis during neuronal wiring. There are several cellular processes observed in the developing nervous system that contribute to the establishment of complicated axonal morphology as follows: (A) Unpolarized immature neuron. (B) Formation and growth of the axon. (C) Axon guidance via cell extrinsic cues from target tissue. (D) Innervation of axon to the initial target, and formation of axonal collateral branches. (E) Axonal remodeling by branch retraction and extension. (F) Establishment of final axonal pattern.

2. Axonal Pattering during Development

At particular times during the development of the nervous system, each neuronal cell starts to extend processes (neurites) from the cell body. In many case, a single process continues to grow to become a long extended axonal process. This symmetry braking process is called "neuronal polarization" (Fig. 1) (Dotti *et al.*, 1988). The lengths of axons greatly differ between different types of neurons and are also affected by the cell-extrinsic signals from surrounding tissue. Importantly, surrounding tissues secrete axon guidance molecules that attract axons to or repulse axons from the targets. During development, gradients of axon guidance molecules are generated in the surrounding tissue, and these signals are received by the "growth cone" a specialized dynamic structure consisting of actin and microtubule cytoskeletons that exists at the tip of growing axon (Dickson, 2002). As mentioned above, many neurons extend a

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