The behavior of an individual is determined in large part by the wiring patterns in the nervous system. These patterns are generated by developmental programs that give rise to the right type and number of neurons, the locations of the cell bodies, morphologies of the axonal and dendritic processes, and the synaptic connections that interconnect neurons into neural circuits.

The formation of neural circuits occurs in a series of steps during development. In the first step, a single axon extends from the cell body of the neuron, led by a structure called the growth cone. The growth cone is loaded with cell adhesion molecules that detect guidance cues from the environment to determine the path of migration; both cell–cell interactions and gradients of diffused ligands in the cellular milieu direct the axon to project to the correct target region. Once in the target region, the axon recognizes the right synaptic partner among many candidates to make synaptic connections. At the same time, neurons also elaborate dendrites to cover the appropriate receptive fields. Interactions between neurites control the spacing and overlap between neurons, which altogether generates the precise yet complex patterns of a neural circuit. One of the major challenges remained is to fully understand the molecular mechanisms that give rise to the formation of neural circuits in the central and peripheral nervous system.

Cell adhesion molecules and their downstream signaling play a key role in each step of neural development. The discovery of these molecules, their receptor and ligand pairs, subsequent downstream signaling, and phenotypic outcomes, was aided by combined biochemical and genetic efforts from multiple model organisms. Several notable families of neural cell adhesion molecules include: Immunoglobulin superfamily (IgSF) cell adhesion molecules, leucine-rich repeat (LRR) containing protein family, semaphorins, neurexins/neuroligins, integrins, and laminins. The largest group among these is IgSF cell adhesion molecules, which contain many important molecules that can be further subdivided into IgCAM (e.g., NCAM, DSCAM, cadherins, DCC, Robos), receptor protein tyrosine kinases (e.g., Eph/Ephrins, FGFR), and receptor protein tyrosine phosphatases (e.g., DLAR). The interactions of these proteins are further translated into downstream signaling events, which direct the motility of neurites to be repelled from one another or to form adhesive connections through cytoskeletal remodeling.

This issue of *Cell Adhesion & Migration* brings your attention to several developing topics on cell adhesion and neural circuit assembly. While the role of actin cytoskeleton has been well established in the morphogenesis and migration of axons and dendrites, the study of its importance in presynaptic assembly has been relatively recent. The review by Nelson et al.\(^1\) covers the essential role of actin cytoskeleton in various aspects of synaptogenesis from specifying the sites for presynapse differentiation, formation of terminal arbors, to the assembly of presynaptic active zone and regulation of synaptic vesicle clustering. These roles of actin are initiated by extracellular cues sensed by cell adhesion molecules while regulated by many actin-associated proteins. The key signaling pathways that converge onto actin regulation as well as their implications in presynaptic assembly
are discussed, which provide a broad overview and identify exciting areas for future study.

The review by Wang et al.\textsuperscript{2} takes us on a journey to understand the molecular mechanisms how peripheral axons of vertebrate somatosensory neurons target to precise region of skin where distinct touch stimuli is detected. While the targeting of peripheral axons of somatosensory neurons to skin share similarity with that of central nervous system in basic steps and certain guidance cues, subtype specificity and distinct biological functions require unique strategy for different kinds of somatosensory neurons to adopt different trajectories and form distinct terminal structures. This highlights the challenge of studying cell adhesion and axon guidance in context-dependent manner.

The highly complex yet specific neuronal connectivity provides the structural basis for behavior. However, the molecular mechanisms linking neural circuits to behavior are largely unknown. To this end, \textit{Drosophila} visual system provides a nice paradigm. Many important players underlying the development of \textit{Drosophila} visual system has been identified, most notably cell adhesion molecules such as N-cadherin, DLAR, and Dscam1/2. Some of them have also been found to be implicated in visual behavior. The review by Zhu\textsuperscript{3} summarizes the anatomy, behavioral types, known molecules, and powerful tools to study \textit{Drosophila} visual circuit and behavior. The principle herein is likely to apply to the studies of molecules in other nervous system and behavior.

Together, these reviews provide a current view of some recently developing topics in axon guidance and related neuronal functions that are mediated by cell adhesion molecules and their downstream signaling. Future research will likely bring excitement about discovering additional cell adhesion molecules that are important for neural circuit assembly, identifying their interacting partners and downstream signaling, understanding their context-specific roles in neural development and behavior, and shedding light onto rebuilding neural circuits for repairing neuronal injury and disease.

Finally, I would like to thank the leading experts in this field who kindly contributed to or peer-reviewed this special focus series. Many thanks for your insight and wisdom!

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