During development, neurons find and interconnect with other neurons in a remarkably precise way. The unfolding of neuronal specificity undoubtedly involves a series of highly specific recognition events between individual neurons. What cellular interactions underlie this specific neuronal recognition? What molecules underlie these specific cellular interactions? To answer these questions, we began several years ago to study cell recognition during neuronal development in the grasshopper embryo. Here we review what we have learned from cellular and immunological studies using the grasshopper embryo. Cell recognition at early stages of neuronal development is mediated largely by specific filopodial contacts, and leads to the stereotyped patterns of selective fasciculation. Our results suggest that such recognition is likely to involve the temporal and spatial expression of many different molecules, and our monoclonal antibody studies reveal cell surface antigens whose distribution correlates with these predictions. We end the paper by reviewing our recent studies on the same cellular interactions in the Drosophila embryo, which leads to a consideration of the future prospects for a molecular genetic solution to this problem using Drosophila.

Specific cell recognition occurs throughout much of neuronal development, from cell migration, to the outgrowth of axonal processes, and the formation of specific synaptic connections. The initial question is: during which period of development, and in which species, can these events best be analyzed and manipulated at the cellular and molecular level? Insects have relatively simple nervous systems, which, in addition to their complex brain (10^5 neurons), includes a chain of relatively simple segmental ganglia, each containing about 1000 pairs of neurons. Unfortunately, if we wait until these neurons have formed many of their specific synaptic connections late in embryonic development, even this "simple" nervous system appears hopelessly complex. However, if we look early enough, when only a handful of neurons have sent out processes, then the system is indeed simple and accessible enough to allow us to ask how individual neurons distinguish their appropriate targets amongst a limited population of embryonic neurons.

At these early stages of neuronal development, cell recognition occurs most dramatically at the tips of growing axons, called growth cones, and at their finger-like extensions, called filopodia. Growth cones radiate many filopodia (approx. 0.1 \mu m in diameter, up to 50 \mu m in length) which transiently explore their environment. Many of these filopodia contact other cell surfaces. To some of these surfaces they strongly adhere, and to others their adhesion is much weaker. If adhesion is weak, during the contractile cycle, the filopodium is retracted; if however, its adhesion is strong, then tension in that direction is increased during the contractile cycle and the leading tip of the growth cone advances towards the point of attachment (Bray, 1982; Letourneau, 1982).

Our results in the grasshopper embryo suggest that cell recognition at these early stages of neuronal development is mediated largely by specific filopodial interactions. The high affinity that growth cones and their filopodia show for particular neuronal surfaces gives rise to the stereotyped patterns of selective fasciculation in which growth cones, confronted with a scaffold of axon fascicles, choose particular axon bundles along which to extend.

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We begin by focusing on the analysis and manipulation of a single neuron, called "G", at a single choice point at which it chooses to fasciculate upon a pair of axons, called P1 and P2, in a particular axon bundle, called the A/P fascicle (Raper et al., 1983a, b, c, 1984; Bastiani et al., 1984). The lessons learned from the G growth cone concerning cell recognition, filopodial adhesion, selective fasciculation, and filopodial insertion apply equally well to other growth cones and selective recognition events throughout grasshopper development (Bastiani and Goodman, 1984a, b).

Our results suggest that cell recognition during neuronal development is likely to involve the temporal and spatial expression of many different molecules. We have generated monoclonal antibodies (mabs) which reveal cell surface antigens whose temporal and spatial distribution in the embryo correlate with the predictions of the cellular studies, namely, neurons whose axons fasciculate together share common surface antigens (Kotrla and Goodman, 1984). In order to isolate and characterize the surface molecules implicated by our cellular and immunological studies using the grasshopper embryo, we have shifted our emphasis to cell recognition in the CNS of the Drosophila embryo. Our recent cellular studies which show that the early embryonic development of the fly CNS is largely identical, albeit in a miniature form, to the hopper CNS in terms of the identified neurons (e.g., G) and their selective fasciculation (e.g., A/P fascicle) (Thomas et al., 1984), thus opening the way for future molecular genetic approaches (Goodman et al., 1984).

REFERENCES


