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Molecular approaches to neural development

The completion of the human genome sequence, along with those of several model organisms, puts development at center stage in biology. Genomes may be likened to assembly manuals for new organisms, and the human sequence is of special interest because it contains instructions for making our brains, the source of our mental lives. We will not be able to read these instructions, however, until we understand the underlying principles of developmental biology, and in particular developmental neuroscience.

Fortunately, developmental biologists and embryologists have long been investigating the events that transform a single cell into a complex organism. Over the last century, a great deal has been learned about how different cells and tissues interact and are transformed through the various stages of development. In a series of landmark experiments in the 1920s, Hans Spemann and colleagues identified a small group of mesodermal cells, the organizer, that was predicted to be the source of signals responsible for the induction of neural tissue in the amphibian embryo. Subsequent studies have identified parallel phenomenon in the development of other species, as well as many other examples of inductive interactions in later development.

What has been lacking until recently is the molecular identity of the signals and machinery that mediate these transformations. In the last decade or so, however, developmental neuroscience has been transformed by a combination of genetics and molecular biology, and this special supplement to *Nature Neuroscience* highlights some of the advances in understanding that have emerged from this approach. We have not attempted to produce a comprehensive review of the field, and instead we asked authors to focus on areas that have seen rapid recent progress.

In the first review, Wilson and Edlund propose a unifying hypothesis to explain differences in neural induction between amphibian and amniote embryos (mammals and birds). Two reviews examine the basis of cell fate specification; Lee and Pfaff describe the interacting network of transcription factors that regulates cell fate decisions in the developing spinal cord, while Monuki and Walsh review our understanding of patterning in the cerebral cortex, based on genetic data from both mice and humans. Corbin, Nery and Fishell approach cerebral cortex development from a different angle, explaining how the recent discovery of tangential migration has revised our understanding of the molecular cues that allow cortical interneurons to reach their final destinations.

A striking feature of neural development is the complexity of the decisions necessary to specify multiple cell types and determine their axonal connections. Yu and Bargmann consider the problem of how axons find their way by integrating information from multiple cues. As discussed by Mombaerts, a particularly complicated example of the axon guidance problem arises in the olfactory system, in which neurons expressing a single odorant receptor from a repertoire of about 1000 genes must find their appropriate glomerular targets. The final step in wiring the nervous system is the formation and refinement of synaptic connections, and Zhang and Poo examine the ways in which this process is affected by neural activity.

Perhaps more than most fields, progress in understanding development has been driven by new technical approaches. Examples appear throughout this collection of reviews, but to highlight the point we have included four short articles from researchers who are pioneering the application of new technologies for measuring and manipulating gene expression in the nervous system. Equally important is the ability to visualize developing neurons *in vivo*, and the last review, by Lichtman and Fraser, surveys recent advances in cellular imaging.

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The Editors