NEURAL DEVELOPMENT

Reconciling models of forebrain induction

The debate over the mechanisms involved in neural patterning has deep roots and two early models still have a strong heuristic influence. On the one hand, Spemann and his followers proposed the existence of separate organizers for the head and for the trunk/tail. On the other hand, Nieuwkoop suggested an early signal for the acquisition of an anterior fate and a subsequent transforming signal that specified posterior regions. Most of the recent evidence obtained in mammals has favoured the existence of two organizers. However, as Foley *et al.* argue in *Development*, this might not be the case and a modification of Nieuwkoop's hypothesis could be enough to explain how the induction of rostral structures occurs.

In mammals, the anterior visceral endoderm has been proposed as the presumptive head organizer. On the basis of an analysis of marker expression, Foley *et al*. identified the hypoblast as the equivalent structure in the chick, a finding consistent with early rotation experiments, which revealed an effect of the hypoblast on axial patterning. However, the authors found that grafting the hypoblast in an ectopic location did not induce brain tissue but only a transient expression of neural and forebrain markers, arguing against its role as a head organizer. Moreover, they found that the distortion observed in the rotation experiments could be explained by an effect of the hypoblast not on cell fate, but on cell movements in the epiblast.

The authors propose that early inductive signals lead to the unstable expression of forebrain markers, which acquire a stable character later in development. However, for this event to occur, the prospective forebrain needs to be protected from the posteriorizing influence of the organizer. Foley *et al*. argue that the movements governed by the hypoblast contribute to this protection by maintaining a safe distance between the future forebrain and the organizer. Later, other signals stabilize the anterior fate of those cells and continue to protect them from caudalization. This model, which can explain observations from chick and mouse, bears more resemblance to Nieuwkoop's idea than to the proposal for the existence of two organizers. These findings should lead us to explore whether the mammalian anterior visceral endoderm can also affect cell movements and the nature of the hypoblast-derived signals involved in this phenomenon.

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References and links

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NEURODEGENERATION

More to poly-Q than aggregate formation?

Several neurodegenerative disorders are produced by the abnormal expansion of a glutamine tract in the sequence of proteins specific for each disease. In most cases, the normal function of the vulnerable protein is not known, and it is commonly accepted that the tendency of the mutant version to form protein aggregates, rather than a loss of function, is more directly related to the onset of the pathology. In the case of spinocerebellar ataxia type 6 (SCA6), however, we know that the culprit is the α_{1A}-subunit of the P/Q-type calcium channel, which contains a poly-Q tract in the carboxyl terminus. This raises the possibility that there may be more than aggregate formation to the presence of the poly-Q stretch in SCA6. Indeed, as Restituito *et al*. report in the September 1 issue of *The Journal of Neuroscience*, the expression of a mutant α_{1A}-subunit can alter the kinetic properties of channels made from specific subunit combinations.

The authors used *Xenopus* oocytes to express chimeric α_{1A}-subunits bearing poly-Q tracts of different lengths in combination with different β-subunits. They observed that the presence of a 30-residue poly-Q stretch in the α_{1A}-subunit shifted the activation voltage of the calcium channels to more negative potentials and slowed their inactivation rate. These effects were only seen if the channels included the β_4-subunit, which is highly expressed in the Purkinje neurons — the cell type most affected in SCA6.

It remains to be determined whether a similar effect of the mutation can be found on the native subunit combinations found in Purkinje neurons. As Restituito *et al.* also show in their study, the α_{1A} exon that encodes the poly-Q stretch is expressed at high levels in this cell type, making it entirely possible that the pathological changes in SCA6 may be partly due to the excessive entry of calcium into the Purkinje cells. If SCA6 turns out to be a channelopathy, we would have a new, but familiar, lead to follow in search of a therapy for this disease.

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WEB WATCH

Illuminating GFP

'All you ever wanted to know about green fluorescent protein but were afraid to ask' could well have been the name of the excellent GFP applications page designed by Wallace Marshall at Yale University. This page is a mine of information on GFP and provides plenty of evidence as to why GFP has become one of the most widely used proteins for cellular imaging. There is even an image of *Aequorea victoria,* the jellyfish that provides the source of the protein — a useful addition to those lecture slides. The web page features a very clean, straightforward design with clearly marked categories that link to books, a newsgroup and various applications and suppliers of GFP-related technology.

The future of the past?

A first port of call for those interested in the history of neuroscience should be the Neuroscience History Archives (NHA). This organization promotes, collects and preserves an archive of material relating to twentieth century American neuroscience. The NHA was established in 1980 at the Brain Research Institute, University of California, Los Angeles, with support from the National Library of Medicine and the Alfred P. Sloan Foundation. The organization preserves the papers and records of neuroscientists and their professional organizations, and so promotes and facilitates research and education in the history of neuroscience.

The website for the NHA has links to several related sites such as RETICULUM, the Neurosciences History Resource and the excellent Women in Neuroscience site. Intriguing links on this site lead to brochures published by the Society of American Archivists that provide guidance for donating records and papers to a repository. Food for thought…

Peter Collins