IN THE NEWS

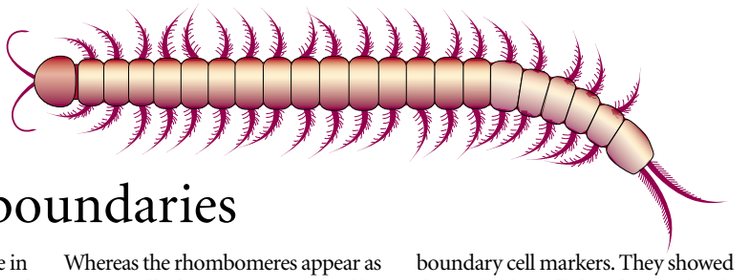
All-singing, all-dancing, and highly controversial **"They can dance on the tip of a needle. They are human life in its earliest, most microscopically and miraculously tiny form: five-day-old embryos that look a bit like blackberries — 200 or so blue–black cells covered in fluff and clustered into a ball"** (*The Observer* UK, 8 July 2001).

'They', or rather, cells derived from them, are also at the centre of a political storm in the USA. The enormous potential of embryonic stem (ES) cells to treat diseases such as Parkinson's and Alzheimer's is not in doubt, there has been intense opposition to ES cell research from pro-life groups, who object to **"destroying what they consider potential human life"** (*Washington Post*, 17 July 2001).

President George W. Bush must decide whether human ES cell research should be funded by federal money. But even his own Republican Party, which traditionally opposes abortion, is divided, some believing that abortion and ES cells are separate issues. Senator Gordon Smith argues: **"Life does not begin in a petri dish; it begins with a mother. Being pro-life means helping the living as well"** (*Washington Post*, 17 July 2001). Nancy Reagan, wife of former president Ronald Reagan, who has Alzheimer's, is also reported to be in favour of human ES cell research (*Times* UK, 14 July 2001).

Opponents of the research argue that adult stem cells might have equal potential. However, the National Institutes of Health issue the following caveat: **"it is impossible to predict which stem cells — those derived from the embryo, the fetus or the adult — will best meet the needs of basic research and clinical applications. The answers clearly lie in conducting more research"** (*Washington Post*, 17 July 2001).

Heather Wood



DEVELOPMENT

Pushing the boundaries

Segmentation is a recurring theme in developmental biology, and most of us are familiar with repetitive structures such as the somites and the hindbrain rhombomeres. In 1993, Puelles and Rubenstein proposed a segmental, or neuromeric, model for the forebrain, based largely on gene expression patterns. But how do the properties of these putative neuromeres compare with those of the rhombomeres? Larsen *et al.* have addressed this question by looking at the developing chick diencephalon.

The diencephalon consists of three subdivisions — the ventral thalamus, the dorsal thalamus and the synencephalon. The dorsal and ventral thalami arise from the parencephalon, which becomes bisected by a prominent boundary, the zona limitans intrathalamica (zli). The subdivisions can be distinguished on the basis of neuronal distribution and axonal projection patterns, as revealed by Nissl staining. However, as Larsen *et al.* show, the diencephalon is not overtly segmented. Whereas the rhombomeres appear as a series of bulges (gyri) separated by ridges (sulci), only the synencephalon is delineated by sulci in the diencephalon. Each rhombomere has a distinct gene expression profile, and the diencephalic subdivisions are similar in this respect. For example, expression of the homeobox gene *Prox* demarcates the synencephalon, whereas expression of *Gbx2* and *Dlx2* is confined to the dorsal and ventral thalamus, respectively. Conversely, as shown recently by the same group, the zli is defined by the absence of *lunatic fringe* (*L-fng*) expression.

The rhombomeres show alternating adhesive properties, with the result that cells do not intermingle between adjacent segments. Lineage restriction between rhombomeres is consolidated by the formation of specialized boundary cells that express chondroitin sulphate proteoglycan (CSPG), tenascin and vimentin. Larsen *et al.* tested whether the diencephalic boundaries also inhibit cell mixing and/or express boundary cell markers. They showed that only the cells bordering the zli and the midbrain–synencephalic junction express boundary markers and present barriers to cell mixing. The boundary between the synencephalon and the parencephalon transiently expresses boundary markers, but the cells from these two territories are able to mix freely.

Larsen *et al.* have shown that the subdivisions of the diencephalon do not fulfil all the criteria that would define them as true segments. So, despite efforts to ascribe neuromeric properties to other regions of the developing nervous system, it seems that the segmental pattern of the hindbrain remains the exception rather than the rule.

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References and links

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ATTENTION

Antisense and sensibility

How many of us, sitting in a schoolroom or lecture hall, have struggled to keep our attention from wandering? The parts of the brain responsible for this tricky task include the substantia innominata — literally, the 'substance with no name' — in the basal forebrain, whose cholinergic projections to the cortex help us to keep our minds on the task at hand. Turchi and Sarter have used antisense techniques to show that blocking the expression of NMDA receptors in the substantia innominata impairs attention in rats.

The animals were trained on a task that required them to pay attention — they had to press one lever if a light had come on for a short time, and another if no light had come on. If their attention lapsed and they missed the light, they got no reward; equally, they missed out on their treat if they incorrectly signalled that there had been a light. The authors then infused antisense oligonucleotides against NR1 subunits of the NMDA receptor into the substantia innominata and tested the rats on this task. Twenty-four hours after the third infusion, the rats were much less able to pay attention to the task — they often signalled that there had not been a light when there had, although they still correctly rejected non-light trials. They were unimpaired, however, on a cued discrimination task that did not test attentional processes.

As the prefrontal cortex sends extensive glutamate projections to the basal forebrain, these results indicate that NMDA receptors in the substantia innominata mediate attentional processes. The pattern of deficit is similar to that produced by lesioning the cholinergic projections from the basal forebrain to the cortex. The authors propose that glutamate inputs act through NMDA receptors to activate these projections, and that this activation is involved in the selection and amplification of specific sensory inputs.

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WEB SITE Sarter's lab