WEB WATCH

Development Down Under

- http://anatomy.med.unsw.edu.au/CBL/Embryo/Embryo.htm

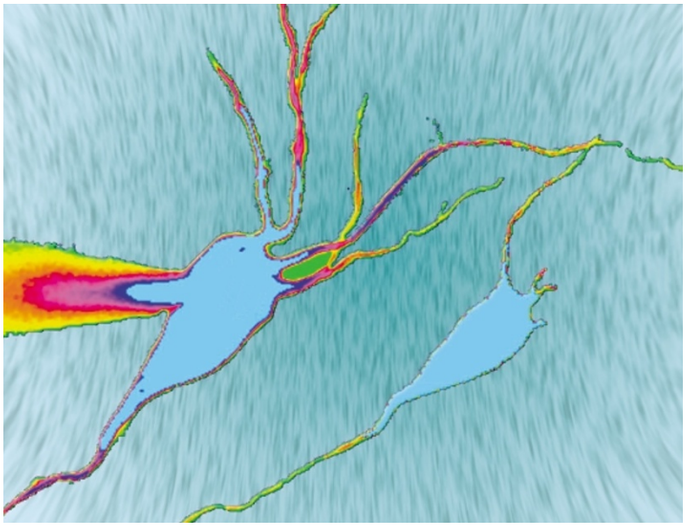
Where can you learn about the basics of developmental biology? There are some excellent textbooks on the subject, but the information is often out of date by the time it becomes available, and the primary literature is so vast that it is impossible to read everything. Mark Hill from the University of New South Wales in Sydney, Australia is attempting to address this problem with a website devoted to the subject.

On the homepage, you can watch a human embryo grow before your eyes, and see the results of Hill's "third successful embryology experiment", his son Christopher. The site focuses mainly on human development, but a range of vertebrate and invertebrate animal models are also presented. There is a basic introduction to human development that is really aimed at school children, although some grown-ups might find this useful too.

The more advanced notes include pages on neural development, as well as separate pages discussing neural crest and sense organs. The site is continually updated, and September 2001 saw the introduction of a section on the development of cerebrospinal fluid. The notes are not especially detailed, but there are plenty of external links if you want to find out more. Many of the principles described are illustrated in the 'Movies' section. Neuroscientists will be particularly interested in the time-lapse movies of neural crest cell migration from Paul Kulesa.

It is clear that parts of the site are still under construction, and it is not always easy to find the relevant information. However, it is certainly a brave attempt to bring all of this information together, and we hope that it will continue to develop to provide a valuable resource.

Heather Wood



A pair of dye-coupled hippocampal neurons. Courtesy of D. Schmitz, University of California San Francisco, USA.

SIGNAL PROCESSING

Closing the gap

It seems that the more we find out about the nervous system, the more we have to overturn our old models in favour of newer, more complex ones. The simple idea of an axon as a fairly passive transmitter for the output of a neuron is gradually being eroded as evidence accumulates that axons have a more active role in signal processing and integration. Schmitz and co-workers add to the story with the demonstration that the axons of hippocampal neurons are electrically coupled by gap junctions.

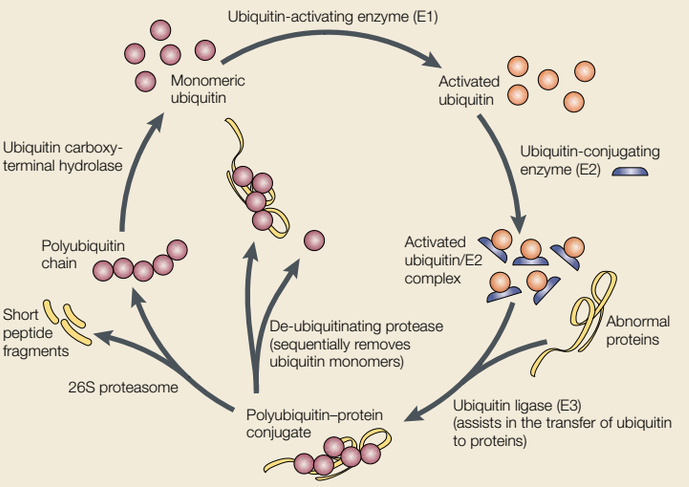
Hippocampal pyramidal and granule cells show small, rapid somatic depolarizations known as 'spikelets'. These had been assumed to arise from attenuated dendritic action potentials, although more recently it was suggested that they were related to electrical coupling. Schmitz *et al.* carried out a detailed analysis of these spikelets and showed that stimulation of the axon of a neighbouring neuron often gives rise to spikelets in the soma of a pyramidal cell. Propagation of the spikelet to the soma depends on activation of fast Na^+ channels in the axon of the recorded neuron, and the generation of spikelets in the recorded neuron by the action potential in the stimulated neuron is reduced by the use of carbenoxolone and other manipulations to prevent gap junction transmission.

The authors proposed that the signal was transmitted from one axon to the other through gap junctions linking them. Further evidence for this idea came from an experiment in which spikelets were recorded in the axons of pyramidal cells after nearby axonal stimulation of another neuron. These spikelets preceded those recorded from the cells' somata.

Schmitz *et al.* also looked for structural evidence of axo–axonal gap junctions. They found pairs of dye-coupled pyramidal cells with clearly separated somata, showing that the cells' somata could not be coupled

SYNAPTOGENESIS

A balancing act



The ubiquitin–proteasome system (UPS) is essential for the degradation of damaged proteins in eukaryotic cells. Although the general function of this system has been characterized in detail in many cell types, we don't know much about its role in neurons. Some reports have linked the UPS to conditions such as Parkinson's disease and Angelman's syndrome, and others have pointed to its direct involvement in synaptic plasticity. A recent paper by DiAntonio *et al.* raises the intriguing possibility that the UPS might participate in synaptic development in *Drosophila*.

The authors screened a collection of flies that overexpressed endogenous genes, looking for mutants in which the structure of the neuromuscular junction was abnormal. DiAntonio *et al.* observed that overexpression of *fat facets* (*faf*), a de-ubiquitinating protease that antagonizes the action of the UPS, led to synaptic overgrowth and diminished transmitter release. Moreover, the authors showed that overexpressing a de-ubiquitinating protease from yeast had a similar effect, indicating that synaptic growth and function do depend on the UPS.

What are the molecular pathways that are affected by *faf*? To answer this question, DiAntonio *et al.* searched for lethal enhancers of the phenotype and identified *highwire* (*hiw*). The *hiw* transcript encodes a putative member of the ubiquitin ligase family — proteins that transfer activated ubiquitin to abnormal proteins, targeting them for degradation. The phenotype of loss-of-function *hiw* mutants was similar to that observed in flies that overexpressed *faf*, pointing again to