IN BRIEF

BRAIN REPAIR

Functional connections are established in the deafferented rat spinal cord by peripherally transplanted human embryonic sensory neurons.

Levinsson, A. *et al. Eur. J. Neurosci.* **12**, 3589–3595 (2000).

Embryonic human sensory neurons were grafted in place of adult rat dorsal root ganglia. The grafted cells extended processes that invaded the dorsal horn, forming branches and then synaptic contacts with host neurons. In addition, the cells were capable of evoking polysynaptic reflexes in the ventral roots, revealing an significant degree of functional integration. This highlights the potential of human embryonic sensory neurons for tissue repair.

CELL BIOLOGY OF THE NEURON

Oligomeric tubulin in large transporting complex is transported via kinesin in squid giant axons.

Terada, S. *et al. Cell* **103**, 141–155 (2000).

The transport of fluorescent tubulin was measured in real time in the squid giant axon. Contrary to previous ideas, tubulin transport was found to depend on kinesin, a microtubule-based motor, and not on actin-based motors. Furthermore, by using fluorescence-correlation spectroscopy, the authors obtained an estimate of the number of fluorescent molecules transported in a complex and observed that tubulin is not transported as a stable polymer, as previously thought, but as a smaller oligomer.

WORKING MEMORY

Synaptic mechanisms and network dynamics underlying spatial working memory in a cortical network model.

Compte, A. *et al. Cerebral cortex.* **10**, 910–923 (2000).

A network model accounting for the persistent activity observed in the prefrontal cortex during spatial working memory tasks. The current model shows bistability between a resting state with low frequency, spontaneous firing, and a spatially-structured state with higher-frequency firing. This is achieved by a combination of an overall recurrent inhibitory influence and NMDA receptor-mediated recurrent synaptic excitation, features not present in previous pattern formation models.

DEVELOPMENT

Cell interactions within nascent neural crest cell populations transiently promote death of neurogenic progenitors.

Maynard, T. M. *et al. Development* **127**, 4561–4572 (2000).

During neural crest cell migration, early, but not late, migratory populations have neurogenic potential. This study shows that neurogenic precursors that fail to disperse early die as a result of cell–cell interactions. Caspase inhibitors prevent this death. Cells that migrated successfully during the early period were no longer susceptible to the influence of cell contact. This was partly mediated by Notch–Delta interactions, and may be a mechanism for assuring that late migratory populations lack neurogenic potential.

NEURODEGENERATION

Multi-purpose presenilins

The recent discovery of nicastrin as a partner for presenilin highlighted once again the putative proteolytic role of this protein and its identity as γ-secretase. However, there seems to be more to the role of the presenilins than just cleaving the amyloid precursor and other membrane proteins. For example, presenilins can affect calcium homeostasis, presumably by potentiating the inositol-1,4,5-trisphosphate ($Ins(1,4,5)P_3$)-mediated Ca^{2+} release from intracellular stores. Yoo *et al.* have tried to gain further insight into the actions of the presenilins on calcium dynamics by focusing on a process tightly linked to Ca^{2+} release from intracellular pools — capacitive calcium entry (CCE).

When intracellular stores release their calcium contents, CCE takes place through plasma membrane channels presumably activated by the $Ins(1,4,5)P_3$ receptor itself . This extra intracellular calcium is then used to replenish the stores. Yoo *et al.* found that CCE (and no other routes of calcium influx) is modulated by the presenilins. In the absence of presenilin-1, or in the presence of an inactive form of this protein, CCE was enhanced in cultured neurons. Conversely, presenilin mutants that increase the production of the amyloidogenic peptide Aβ42, attenuated CCE. Furthermore, the putative CCE-associated current I_{CRAC} was also reduced in the presence of the 'gain-of-function' mutant presenilins.

An intriguing finding in this study was the fact that blocking CCE by pharmacological means increased the production of Aβ42, an effect dependent on the presence of a functional presenilin-1. However, increasing Aβ42 by other manipulations did not lead to a reciprocal change on CCE amplitude. These observations indicate that the modulation of CCE by the presenilins may be an event upstream of γ-secretase activity, pointing to this route of calcium influx as a possible target for therapeutic approaches against Alzheimer's disease.

It will be important to establish the actual mechanism whereby presenilins affect CCE. Do they modulate calcium entry by proteolysis of a modulatory element? If this were the case, it would expand the list of molecules susceptible to the action of the presenilins and it would point to a more general role for these molecules in the metabolism of membrane proteins.

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References and links

ORIGINAL RESEARCH PAPER Yoo, A. S. *et al.* Presenilin-mediated modulation of capacitive calcium entry. *Neuron* **27**, 561–572 (2000)

FURTHER READING Vassar, R. & Citron, M. Aβ-generating enzymes: recent advances in β- and γ-secretase research. *Neuron* **27**, 419–422 (2000) | Yu, G. *et al.* Nicastrin modulates presenilin-mediated *notch/glp-1* signal transduction and βAPP processing. *Nature* **407**, 48–54 (2000) | Berridge, M. J. *et al.* The versatility and universality of calcium signalling. *Nature Rev. Mol. Cell Biol.* **1**, 11–21 (2000)

WEB SITE The Alzheimer's web

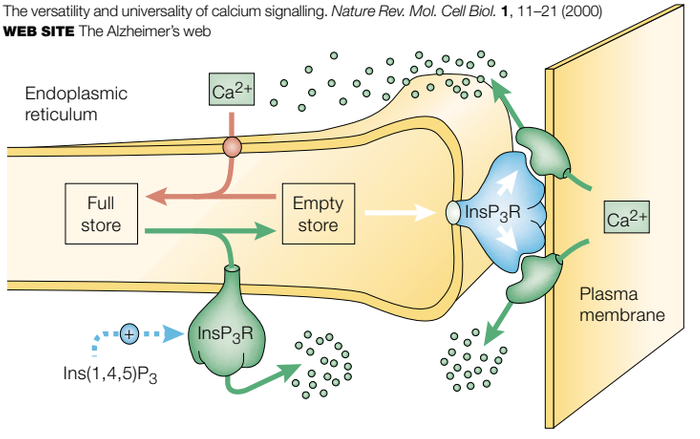

Figure adapted from Berridge, M. J. *et al. Nature Rev. Mol. Cell Biol.* **1**, 11–21 (2000).