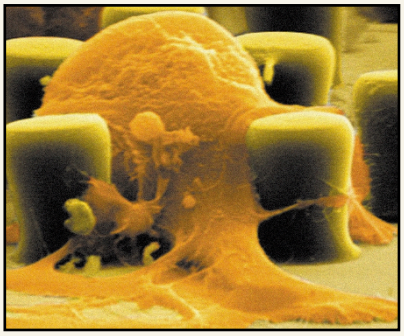
Neurons go *in silico*



Understanding how neural networks operate remains one of biology's greatest challenges. However, researchers have a limited set of tools with which to work, being forced either to record neuronal activity directly using fine electrodes or to model neural networks *in silico*. In an extension of previous studies using non-neuronal cells (*Nat. Biotechnol.* **19**, 121–124, 2001), Peter Fromherz and Gunther Zeck reveal that they have been able to combine microelectronics and cell biology to create a neuron chip suitable for monitoring neuronal activity (Proc. Natl. Acad. Sci. USA **98**, 10457–10462, 2001). The researchers grew neurons from the snail *Lymnaea stagnalis* on silicon-coated microchips, which have a stimulus-generating region and a detector region. The researchers used microscopic "picket fences" (see photo) to prevent the neurons shifting from these areas as they grow on the chips. The chip was used to record synaptic activity between pairs of snail cells, which agreed with the voltage changes recorded using intracellular electrodes. Fromherz says that the next step is to develop "chips incorporating chemical synapses, and to create cellular prosthetic devices in which two disconnected neurons can be coupled through the chip." *LF*

Virus-induced cell death

Adeno-associated virus (AAV), which is frequently used as a vector for gene therapy, may also be used to selectively destroy cancers, according to Peter Beard and colleagues at the Swiss Institute for Experimental Cancer Research (*Nature* **412**, 914–917, 2001). Viral-based cancer therapies (so-called oncolytic viruses) infect cells, but they can only replicate and lyse cancerous cells lacking active p53, a tumor-suppressor protein. However, existing oncolytic viruses incorporate an adenovirus, which has been associated with serious side effects. Beard has shown that AAV, which has a better safety profile than adenovirus, can also kill cells lacking functional p53. Ultraviolet-inactivated AAV triggers a "DNA damage response", a general process through which cells check for and eliminate abnormal DNA. AAV arrests the growth of both healthy and tumor cells, but causes apoptosis in only cancerous cells lacking functional p53. Importantly, the cancer-killing effects of AAV were unrelated to viral replication or the expression of viral proteins. AAV protected mice against both established and new adenovirus-induced tumors. Beard is now looking to determine which portion of the AAV evokes the damage response. *LF*

Research News Briefs written by Liz Fletcher, Judy Jamison, and Christopher Martino.

Herbal remedy for toxic waste

Until recently, cleaning up sites contaminated by toxic metals involved either removing the soil or cementing over the affected area. Today, plants that naturally hyperaccumulate metal ions have become a novel means of soil remediation. Scientists at Purdue University (West Lafayette, IN) have now discovered and cloned the genes conferring the nickel-accumulating properties on wild mustard, *Thlaspi goesingense* (*Proc. Natl. Acad. Sci. USA* **98**, 9995–10000, 2001). The metal-accumulating proteins involved—members of the cation-efflux family—are encoded by a single genomic sequence *TgMTP1* (for *T. goesingense* metal tolerance protein). The protein sequesters the heavy metals within the vacuoles of shoots, where they cannot harm the plant. These TgMTP1 proteins have homologs in yeast, mammals, and bacteria, and all are involved in transporting metal ions including nickel, zinc, cobalt, and cadmium. The Purdue investigators further showed that different transcripts of the *TgMTP1* gene had different heavy-metal specificities: one transcript conferred tolerance to cadmium, cobalt, and zinc, whereas the other transcript targeted nickel. Wild mustard is a small and slow-growing plant, and chief investigator David Salt says that scientists will likely have to transfer the relevant genes into high-biomass, fast-growing plants such as grasses. *JJ*

Biosensors unhinged

Homme Hellinga and colleagues at Duke University (Durham, NC) and the Naval Research Laboratories (Washington, DC) have developed a biosensor that harnesses the natural flexibility of ligand-binding proteins (*Science* **293**, 1641–1644, 2001). The team used a bacterial protein possessing a molecular hinge that swings shut when the protein binds the sugar maltose. One end of the protein was anchored to an electrode surface, while the other was linked to a redox complex incorporating ruthenium red. When the protein binds the ligand, the lid closes, drawing the redox complex away from the electrode surface and creating a measurable change in voltage difference. The team adapted bacterial proteins to bind to maltose and used this system to measure its concentration in beer, proving that the system is sufficiently robust to cope with real-life situations. Hellinga says that his laboratory will use computational methods to redesign the ligand specificity of the protein-based sensors, and potentially to manipulate their affinities for ligands. Such biosensors could be applied to medicine, environmental monitoring, and defense. *LF*

Let there be EG-VEGF

All known stimulators of vascular growth do so regardless of their tissue of origin. This has confounded scientists hoping to develop tissue-specific modulators of angiogenesis. Now, Jennifer LeCouter and a team of scientists from Genentech (S. San Francisco, CA) have discovered the first tissue-specific regulator of angiogenesis, so-called endocrine-gland-derived vascular endothelial growth factor (EG-VEGF; *Nature* **412**, 877–884, 2001). EG-VEGF stimulates angiogenesis in endocrine glands (e.g., ovaries, testes, adrenal glands, and placenta), without effect on endothelial cells in other tissues. Inhibition of EG-VEGF could therefore be used to block, for example, the growth of ovarian tumors. The discovery of EG-VEGF suggests that other tissue-specific angiogenic molecules exist. If other such specific molecules are found, coauthor Napoleone Ferrara states, "these may in turn have considerable therapeutic potential." Once such molecules have been found, opportunities will arise for promoting or stifling angiogenesis in diseased tissues without affecting healthy ones. With such potential, Ferrara concludes, "These molecules should be the object of an intense search." *CM*