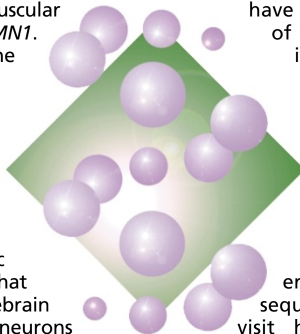
TOUCHING**base**

No *Naip*: naff neuroprotection

As has been previously reported in these pages, the gene encoding the neuronal apoptosis inhibitory protein (NAIP) is implicated in modulating the severity of spinal muscular atrophy—a disorder caused by the mutation of *SMN1*. These genes are juxtaposed on chromosome 5 in the human and 13 in the mouse, and so it comes as no surprise that a few lesions that affect *SMN* also compromise the integrity of *NAIP*. Several studies collectively point to a role for *NAIP* in protecting neuronal cells against apoptosis induced by insult to the nervous system. First, the NAIP sequence indicates its membership of a family of proteins that inhibit apoptosis, and *in vitro* studies demonstrate its anti-apoptotic effect. Subsequently, Diagen Xu *et al.* showed that transient ablation of the blood supply to rat forebrain results in an elevation of *Naip* expression in those neurons that survive the insult. They also found that injecting agents that increase neuronal levels of Naip reduce the extent of damage in the rat hippocampus. In contrast with the single copy of *NAIP* found in the human genome, there exist as many as six discrete *Naip* genes in the mouse. Martin Holcik and colleagues, of the Children's Hospital of Eastern Ontario Research Institute, now describe the effect of knocking out one of these, *Naip1*, which is expressed in mouse brain (*Proc. Natl Acad. Sci. USA* **97**, 2286–2290; 2000). They find that the mutant mice develop normally, but lose many more hippocampal neurons than do wild-type mice when induced to have epileptic seizures. Exactly how and to what degree ablation of NAIP levels combine with the loss of SMN activity to produce an exacerbated spinal muscular atrophy remains to be determined, although judging from the recent spate of papers that explore the molecular components of the disorder, the answer may not be far off.

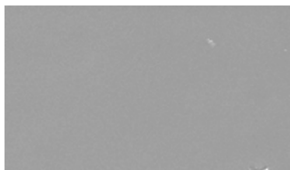
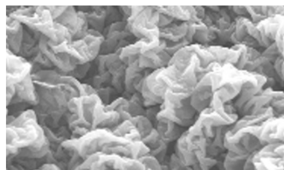


Genomes galore

Nearly lost in the hoopla over the human and model system genome sequences, some lesser-known genome projects have gained momentum in recent months. The genome of the higher fungus *Neurospora crassa*, famous for its ordered octads, and more recently for its circadian behaviour and epigenetics, has been tackled by a number of groups in the United States and Europe. So far, 20,000 expressed sequence tags representing more than 5,000 genes have been obtained, as has an extensive cosmid library (now being used to assemble tiling paths for the entire 43-Mb genome), and a consortium in Germany is sequencing two of the seven chromosomes. Several proposals for finishing the genome by shotgun sequencing are under review. For more information, visit http://www.fgsc.net/outlink.html or attend this month's *Neurospora* 2000 ('N2K') conference in Asilomar, California (March 9–12). In a more applied vein, Orion Genomics LLC of St. Louis, Missouri has announced its plans to apply its proprietary technology to the genome of *Brassica napus*—commonly known as canola—one of the world's leading oilseed crops. The attraction of canola (as a candidate for genome-sequencing) is heightened by its close relation to another member of the Brassica family, *Arabidopsis thaliana*. Although the canola genome is larger than that of its model–system cousin by an order of magnitude, Orion believes that the use of GeneThresher™ technology—which involves filtering of genomic clones by methylation state to subtract repetitive sequences (*Nature Genet.* **20**, 305–308; 1999)—will enable quick sorting of the genes from the chaff, as well as providing grist for a comparative analysis of the canola and *Arabidopsis* genomes.

Honey, I shrunk the chips!

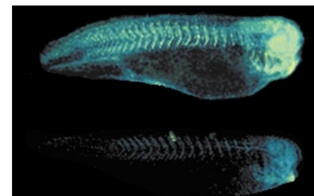
The availability of suitable target for microarray analysis sometimes limits the extent of analysis. And so the size of the microarray—its physical dimensions—can be critical to success: the smaller the surface that supports accessible probe, the smaller the requisite amount of target. Kurt Halverson, Douglas Astry and colleagues, of the 3M Bioanalytical Technologies Project (St. Paul, Minnesota), are developing a method for making microarrays that addresses this concern, in addition to other issues, such as integrity of signal. They have concocted an attachment coating comprised of modified polyacrylamide that supports the covalent attachment of high concentrations of DNA in a three-dimensional mesh. The coating is spread onto shrinkable film to a depth of 1 μm, after which probes are spotted onto it. (Consistent, thin coverage is enabled by the same technology 3M uses to make photographic film.) Halverson points out that if one wishes to obtain a stronger signal than that afforded by two dimensions, "the only way is up" [from the solid surface]—a realization that is also exploited by Motorola, Inc., which is developing microarrays wherein probes are embedded in blocks of gel (see *Nature Genet.* **19**, 317; 1998). The first set of feasibility studies carried out by the 3M group indicates that spots of uniform 500-base probe withstand the heat-shrinking process and generate intense signal upon hybridization with radioactive target. Moreover, electron-scanning images of coated film, pre- and post-shrinking (see inset), show that, contrary to early fears of Halverson and colleagues, the coating doesn't pop off the film when the latter shrinks: rather, it ruffles. This means that microarrays generated through standard robotic procedures might be shrunk to a fraction of their current size—and macroarrays (for example, measuring 8×12 cm^2), which are easier and faster to make than standard spotting glass-slide arrays, can be shrunk to about 1.5×2.5 cm^2. Clearly, the technology must be further developed before it can be put to routine use; the fact that 3M is now funding the research (the National Institute of Technology and Standards funded the pilot studies) indicates their faith in the approach.

Turning up the heat. Electron-scanning micrograph of acrylamide-coated plastic: before (left) and after (right) application of heat (150 °C for 30 s).

Brightening up *in vivo* imaging

Studies of gene expression patterns typically rely on *in situ* hybridization or colorimetric staining assays, both of which require processing to make the subject transparent. In March's issue of *Nature Biotechnology*, Thomas Meade and colleagues describe an improved way of tracking gene expression in living organisms using magnetic resonance imaging. The 'brightness' of magnetic resonance images depends on contrast reagents. The authors have engineered a contrast reagent, called EgadMe, that is activated by the commonly used marker enzyme β-galactosidase. By injecting EgadMe, together with either RNA or DNA encoding β-galactosidase, into *Xenopus* embryos at the two-cell stage, Meade and colleagues were able to probe embryonic structures at a deeper level and higher resolution than is permitted by light microscopy. They are now developing contrast reagents that can be delivered into the cell's interior without injection, with the ultimate goal of tracking gene expression in real time in developing embryos.



In living technicolour. Brighter images of *Xenopus* embryos injected with β-gal mRNA and EgadMe (top) compared with EgadMe alone (bottom).

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