

Toxic neighbors

Mutant forms of the detoxifying enzyme Cu-Zn superoxide dismutase (SOD1) account for one-fifth of all dominantly inherited cases of amyotrophic lateral sclerosis (ALS), a debilitating neurodegenerative disorder affecting adult motor neurons. Although mutant SOD1 is known to be toxic, it is unclear whether it acts directly in motor neurons to promote their death or whether damage to nonneuronal cells is the crucial event in disease progression. New work by Don Cleveland and colleagues (*Science* 302, 113–117; 2003) now implicates nonneuronal cells as the source of SOD1-induced toxicity in a mouse model of ALS. The authors generated chimeric mice containing mixtures of wild-type cells and cells expressing one of several mutant forms of SOD1 that produce ALS-like symptoms when expressed systemically. Notably, they found that motor neurons expressing mutant SOD1 survived longer in the presence of wild-type nonneuronal cells. Conversely, wild-type motor neurons showed classic signs of degeneration when positioned adjacent to nonneuronal cells expressing mutant SOD1. The protective effect of nonneuronal cells expressing wild-type SOD1 could have important therapeutic applications in delaying motor neuron degeneration and disease progression in individuals with ALS. **KV**

Human protein-protein catalog

Keeping track of the networks of confirmed protein-protein interactions is a daunting task that requires labor-intensive sifting through mountains of published work. Many interactions are inferred from colocalization data or bioinformatic sequences; others are experimentally confirmed. Now Akhilesh Pandey and colleagues report the development of the Human Protein Reference Database (HPRD), an online searchable catalog of confirmed protein interactions (*Genome Res.* 13, 2363–2371; 2003). The database allows a user to search for a protein and call up a visual web of interacting proteins. Manual curation of the database allows the inclusion of information that is not included in other protein databases like SWISS-PROT. Information on known post-translational modifications, subcellular localization and tissue distribution and how such states affect the protein's behavior *in vivo* are included in this database in an attempt to be comprehensive. The documented interactions are linked directly to PubMed citations that will allow the user to find additional information about how the interaction was determined. There are currently 3,000 proteins in the database, and information on their roles in human disease is included. The curators estimate that that number will grow to 10,000 by the end of the year. (Visit the HPRD at <http://www.hprd.org>.) **MS**

Signature of the Prisoner's Dilemma

The Prisoner's Dilemma is a classic theoretical scenario that illustrates the nature of the incentives for cooperative social behavior. Duncan Greig and Michael Travisano now report that the evolution of the genome of *Saccharomyces cerevisiae* may be influenced by a yeast version (*Proc. R. Soc. Lond. B* advance online publication, 9 October 2003; doi:10.1098/rsbl.2003.0083). In the classic Prisoner's Dilemma, cooperation gives the greatest average benefit to both players, whereas 'defection' gives the greatest individual advantage (to the defector). In studying the highly polymorphic yeast *SUC* gene family, Greig and

Travisano noted that there might be a similar dynamic at work. The *SUC* genes encode an invertase, a secreted enzyme that hydrolyzes sucrose. The authors found that in a small population, the defector (a cell lacking *SUC2*) is less fit, whereas in a large population, the defector is more fit, consistent with the 'incentive' to try to get something for nothing (stealing sugar without contributing the enzyme). This "instability of cooperation" is a hallmark of the Prisoner's Dilemma, and Greig and Travisano suggest that the polymorphic nature of several yeast genes encoding secreted proteins may reflect the variable nature of social interactions. **AP**

Huntingtin's role in axonal transport

Huntington disease is caused by polyglutamine expansions in the huntingtin protein. Mutant huntingtin self-aggregates, sequesters other proteins and can translocate into the nucleus. Accumulation of poly-Q proteins in the nucleus, but not in the cytoplasm, leads to neuronal and, ultimately, organismal death. In a recent paper, Shermali Gunawardena and colleagues present work suggesting that cytoplasmic accumulation of poly-Q proteins leads to blockage of axonal transport (*Neuron* 40, 25–40; 2003). Working with flies, the authors knocked down wild-type huntingtin expression using RNAi. These flies had axonal blockages that were further enhanced by reductions in motor proteins involved in axonal transport. Using transgenic models, the authors showed that pathogenic poly-Q proteins led to organelle accumulations characteristic of axonal transport defects. Moreover, these fly embryos had lower concentrations of soluble motor proteins, suggesting that poly-Q proteins can deplete them, perhaps by sequestering them into poly-Q aggregates. These findings indicate that normal huntingtin is required for axonal transport and that whereas mutant huntingtin in the nucleus leads to apoptosis, poly-Q aggregates in the cytoplasm result in defective axonal transport. **DG**

Hanging on til the bitter end

Abscission, the programmed shedding of unwanted leaves, flowers or fruits from the plant body, has been poorly studied at the molecular level. Melinka Butenko and colleagues recently identified the molecular basis of a unique *Arabidopsis thaliana*



mutant that is completely defective in the last step of floral abscission (*Plant Cell* 15, 2296–2307; 2003). The *A. thaliana* inflorescence deficient in abscission (*ida*) mutant retains all floral parts indeterminately, even to the point of sporting senescent organs after the shedding of mature seeds. The mutation is caused by a T-DNA insertion into *IDA*, a gene encoding a novel secreted protein that may be part of larger family of putative ligands in plants. The gene is expressed specifically in the floral abscission zone, an anatomically distinct structure that constitutes the region where organs detach from the plant body. Cells in the abscission zone of *ida* mutants begin the process of cell wall dissociation but don't complete it, suggesting that an *IDA*-dependent signal is required. Butenko *et al.* propose that *IDA* could be a ligand for *HAESA*, a receptor previously shown to be involved in floral organ abscission. **AP**

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