

NEUROSCIENCE

Long-Term Memory: A Positive Role for a Prion?

Prions are famous evildoers. These proteins, which are thought to be misfolded versions of normal ones, cause deadly neurodegenerative diseases, including “mad cow disease,” in mammals. In yeast, however, prions are largely benign, if nonfunctional (*Science*, 2 August 2002, p. 758). Now, a team led by neuroscientist Eric Kandel and postdoc Kausik Si at Columbia University College of Physicians and Surgeons in New York City may have discovered the first positive function for a prionlike protein: the formation of long-term memories.

In two papers in the 26 December issue of *Cell*, the Columbia researchers, along with Susan Lindquist of the Whitehead Institute in Cambridge, Massachusetts, show that cytoplasmic polyadenylation element binding protein (CPEB) is required for cementing cellular long-term memories in neurons of the sea slug *Aplysia*. In yeast, the papers show, this same protein acts like a prion, and its prion form appears to be the one active in memory formation.

The work has led to the radically new notion—which is far from proven—that prionlike changes in protein shape may be a

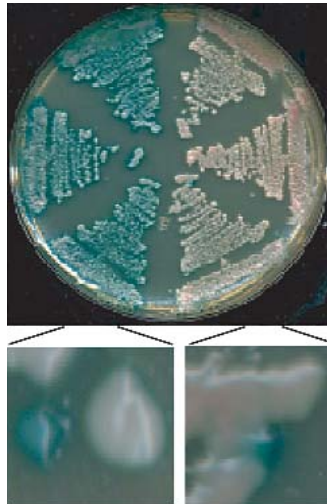
key molecular event in the formation of stable memories. Neuroscientist Solomon Snyder of Johns Hopkins University in Baltimore, Maryland, calls the work “a breath of fresh air.” He adds: “It’s the first truly novel concept about a molecular mechanism for learning and memory in perhaps 30 years.” If the work holds up, it will broaden scientists’ views of prions, hinting that they could play roles in development and other body functions that require long-lasting proteins, a hallmark of prions.

Kandel had no inkling he’d end up with a prion when he and his colleagues began investigating a mystery of memory a few years ago. In *Aplysia* neurons, they had

found that repeatedly spritzing one branch of a sensory neuron with the neurotransmitter serotonin induces cellular changes that underlie long-term memory in that neuronal branch but not in a second branch of the neuron. But the neuron appeared to be sending the messenger RNAs (mRNAs) needed to synthesize the required memory-forming proteins to all

its branches. So in some unknown way, the serotonin input apparently marked the affected branches so that only they could use the mRNAs.

Si set out 3 years ago to determine the nature of this mark. He was interested in CPEB because it was known to activate mRNAs, chemically preparing them to be translated into proteins, and because it springs into action when neurons are stimulated. Indeed, Si soon found support for the idea that CPEB is the mark. Pulses of neural activity caused *Aplysia* neurons to produce many copies of CPEB in the stimulated nerve terminals. In addition, selectively blocking CPEB production caused the persistent cellular changes that underlie long-term memory to ▶



Switchover. Yeast cells (top) with active CPEB are blue, inactive CPEB white. But inactive CPEB can flip into an active, prionlike form, producing blue cells (right), and the reverse conversion can also occur (left).

SCIENTIFIC CONDUCT

Charges Don't Stick to *The Skeptical Environmentalist*

COPENHAGEN—Danish statistician and environmentalists’ bête noire Bjørn Lomborg has won a major victory in his fight to rehabilitate his reputation as a scholar. Last month, Denmark’s science ministry repudiated an earlier finding by one of its committees that Lomborg’s controversial 2001 bestseller, *The Skeptical Environmentalist*, is “scientifically dishonest.”

The Danish Research Agency’s Committee on Scientific Dishonesty (DSCD) launched an investigation in mid-2002 into allegations that Lomborg selected sources to fit his views. For example, he was accused of disregarding known extinction rates when estimating species loss and glossing over uncurbed population growth in some regions when discussing the reassuring implications of a global slowdown in population. After the DSCD issued its ruling last year (*Science*, 17 January 2003, p. 326), Lom-



Victim? Bjørn Lomborg accuses critics of mudslinging.

borg, head of Denmark’s Institute for Environmental Assessment, filed a complaint with the ministry.

In an 18 December 2003 ruling signed by section chief Thorkild Meedom, the ministry found DSCD’s findings flawed on several counts. It held that DSCD’s legal mandate is to rule on allegations of fraud, not on accusations of failure to follow “good scientific practise.” It also criticized DSCD’s ruling for lacking documentation, for failing to document the argument that the book is dishonest, and for describing Lomborg’s research in unduly emotional terms. The ministry did not evaluate the soundness of the science or the claims in the book.

The ruling leaves DSCD officials chagrined. It’s “exceedingly tough and [made] in an unforgiving tone which is unprecedented,” says committee chair Henrik Waaben, a high-court judge. He notes that the ruling does not vindi-

cate *The Skeptical Environmentalist* and says that DSCD may yet reexamine the original complaints. Ecologist Stuart Pimm of Columbia University, one of three original complainants to DSCD, says he’s not surprised by the ruling. But rather than an exoneration, Pimm calls it “a pardon from the political leadership.”

Not surprisingly, Lomborg, who labels the case against him “infected from the beginning,” sees it differently. The ruling “sends a clear message that sound arguments are necessary. Mudslinging isn’t enough,” he told *Science*.

The ultimate loser may be DSCD. Jens Morten Hansen, director of the Danish Research Agency, says that standards of good scientific practice should vary by field. “The Lomborg case shows that social scientists should not be judged within the same framework as natural scientists,” he argues. Later this month, the agency is expected to release new rules for investigating complaints against scientists that could call for a shake-up of the dishonesty committee.

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