# EDITORS' CHOICE

edited by Gilbert Chin

MICROBIOLOGY

## Two in One

Bovine spongiform encephalopathy (BSE, commonly referred to as "mad cow disease") is thought to involve the transmission of a pathological conformation of an endogenous prion protein, which exists in cellular ($PrP^{C}$) and scrapie-inducing ($PrP^{Sc}$) forms. How a single host can harbor multiple strains of this infectious agent is unclear. In the intact animal, this question is complicated by the fact that each strain may manifest itself in a different type of cell and that strain variations then might be intermingled with differential protein processing.

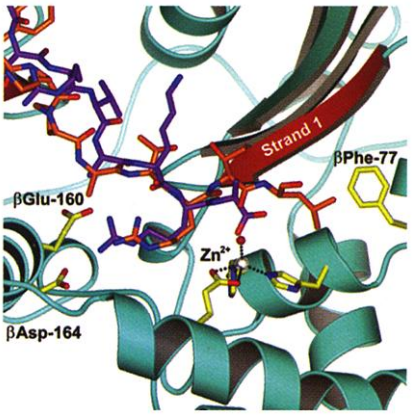
Birkett *et al.* have described the propagation of strain-specific characteristics within a single scrapie-susceptible cell line. Treatment of a scrapie-infected mouse cell line with the drug pentosan sulfate eliminated traces of the pre-existing $PrP^{Sc}$. Subsequent infection with a second strain of scrapie (with distinct biochemical properties and a different disease incubation time when transmitted to mice) yielded a cell line that exhibited characteristics of the newly introduced scrapie strain, rather than that of the original. This finding begs the question as to precisely how strain specificity can be maintained within a single cell type, but the development of this model system should allow researchers to pose detailed questions about prion strain variation. — SMH

*EMBO J.* **20**, 3351 (2001).

CELL BIOLOGY

## Stretched for the Guillotine

The presence of many membrane-bounded compartments in a eukaryotic cell means that proteins must have signal sequences that target them to the appropriate organelle and that organelles must have translocation machinery to import these proteins. Although the signal sequences appear to adopt an α-helical conformation during translocation, Taylor *et al.* show that the mitochondrial processing peptidase—a thermolysin-like zinc-dependent protease—recognizes an extended or β strand–like conformation of the signal sequence. The peptidase active site utilizes both position-dependent binding sites for arginine and aromatic side chains as well as main chain interactions with the edge of a β sheet in order to accommodate the wide variety of sequences. — GJC




**Signal sequence peptides (purple, orange) positioned by β-strand 1 (red) near the catalytic Zn (white).**

*Structure* **9**, 615 (2001).

CLIMATOLOGY

## Wandering Reefs

Today, coral reefs are found only where the ocean is warm. On this basis, their past distribution (or absence) could be used as a clue to infer continental latitudes on the one hand, or past ocean temperatures on the other, if an independent estimate of latitude through paleomagnetism were available. To test the latter notion, Kiessling analyzed a large data set on the distribution of coral reefs since they arose in the Early Cambrian, for which independent data on paleolatitude are available. The analysis, however, shows that although corals ranged mostly up to about 20° to 40° north or south latitude over time, their distribution did not correspond very closely to paleoclimate. Known warm climates did not always have a broader distribution of reefs, and the reef zone expanded in the Jurassic and again recently (periods of relatively cold climate). In addition, the dominant types of reefs changed during cold or warm intervals, thus confusing a simple response to temperature. — BH

*Geology* **29**, 751 (2001).

PROTEIN DESIGN

## Taking Turns

How do proteins fold into the correct structure—the native state—within a biologically re-

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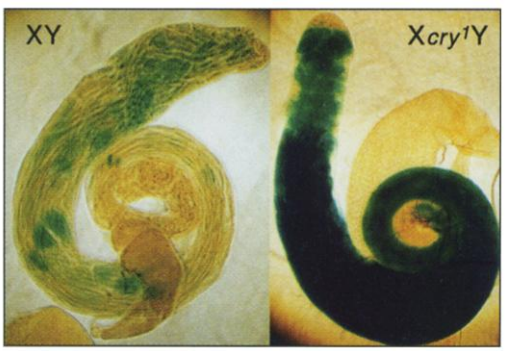



**Expression of *Ste* (green) in testis with (left) and without (right) *Su(Ste)* repeats.**

GENETICS

## Interfering with Male Fertility

Repeated sequence elements play an important role in male meiosis and sperm development in the fruit fly *Drosophila*. One striking example of this is the interaction between the *Stellate* (*Ste*) repeats on the X chromosome and the *Suppressor of Stellate* [*Su(Ste)*] repeats on the Y chromosome, both of which are expressed in the testis. The *Ste* locus consists of tandem repeats of an open reading frame (ORF) encoding a subunit of casein kinase 2. In wild-type male flies, expression of these repeats is somehow repressed by the *Su(Ste)* tandem repeats, which are highly related in sequence to *Ste* but contain nucleotide substitutions that disrupt the ORFs. Male flies with deletions of the *Su(Ste)* repeats overexpress *Ste* and exhibit multiple meiotic abnormalities, including chromosome disorganization and deposition of protein crystals in spermatocytes, which can result in sterility.

Aravin *et al.* show that *Su(Ste)* inhibits expression of *Ste* via an RNA interference mechanism [also known as double-stranded RNA (dsRNA)-mediated gene silencing]. In the wild-type male testis, both strands of *Su(Ste)* are transcribed, leading to production of short RNAs that can target and eliminate the *Ste* transcripts [for more on making small RNAs, see Hutvágner *et al.*, *Science* Express, 12 July 2001, 10.1126/Science.1062961 and Grishok *et al.*, *Cell* **106**, 23 (2001)]. The same gene silencing mechanism also appears to control the level of the *Su(Ste)* sense-strand RNA, creating a negative feedback loop. These results not only explain the molecular basis of the interaction between *Ste* and *Su(Ste)* but also illustrate that RNA interference is a natural mechanism of gene regulation in flies. — PAK

*Curr. Biol.* **11**, 1017 (2001).

SOURCE: (LEFT) ARAVIN *ET AL.*, *CURR. BIOL.* **11**, 1017 (2001); (RIGHT) TAYLOR *ET AL.*, *STRUCTURE* **9**, 615 (2001).

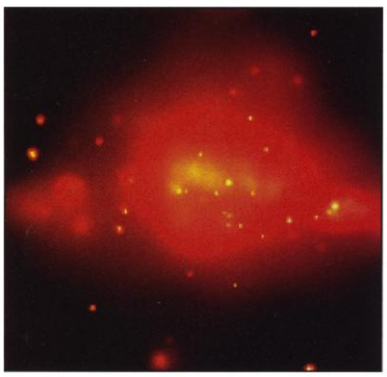
alistic time? According to current understanding, folding occurs on a funnel-shaped free energy surface that is biased toward the native state. Along this funnel, many folding pathways are possible, but the dominant ones are believed to maximize the formation of energetically favorable native contacts while minimizing the loss in configurational entropy as the chain becomes more constrained. To test this view, Nauli *et al.* have redesigned a small protein so that it folds along a different pathway than the wild-type molecule. Protein G is a small protein that contains an α helix and a four-stranded β sheet formed by two β turns. The authors reordered the stability of these β turns and succeeded in inverting the sequence in which these substructures appear in the folding pathway, supporting the idea that protein folding takes the route with the most favorable interactions. — JU

*Nature Struct. Biol.* **8**, 602 (2001).

ASTROPHYSICS

## Galactic Corona from Superbubble Froth

Theory predicts that a typical spiral galaxy, such as the Milky Way, should be surrounded by a corona of very hot gas, but it has been difficult to identify the coronal x-ray signature from our position within the galaxy.



**Corona around NGC 4631.**

Now, Wang *et al.* have detected a corona around the galaxy NGC 4631 using the high resolution and long exposure time afforded by the Chandra X-ray Observatory. The x-ray emission from the coronal gas is enhanced in regions where a froth of superbubbles, created by massive star clusters, have broken out of the plane of the disk, suggesting that the corona is heated by active star formation. The coronal morphology is similar to the radio halo morphology, which indicates that the hot coronal gas may be deforming the magnetic field lines of the galactic disk. — LR

*Astrophys. J.* **555**, L99 (2001).

PHYSICS

## Optical Trains for Atoms

The ability to cool a cloud of atoms to such low temperatures that they form a Bose-Einstein condensate (BEC) and the ability to extract a coherent matter beam from this cloud promise the potential to do with atoms what can be achieved with optical lasers—interferometry, holography, scattering, and spectroscopy. However, full exploitation of the atom laser requires the development of precision atom-optic devices such as mirrors, lenses, beam splitters, and resonators. One distinguishing property of a BEC is that all of the atoms have the same magnetic moment and so experience a force in the presence of an inhomogeneous magnetic field. Under optical stimulation, the magnetic moment of the atoms can be flipped so that the force on the atoms is reversed. Bloch *et al.* use this effect—the switching of the force the atoms experience with optically induced transitions of the magnetic moment—to demonstrate the atom-optic equivalent devices that will help allow the manipulation of coherent atom beams with the same precision and control as that available for optical lasers. — ISO

*Phys. Rev. Lett.* **87**, 030401 (2001).

BIOMEDICINE

## Whooping Back

Before mass vaccination in the 1950s, *Bordetella pertussis* was a major cause of infant death. Despite vaccination, pertussis remains endemic, with a prevalence as high as 1 to 4% and with as many as 30% of people with persistent coughs found to be infected. Mooi *et al.* investigated the apparent reemergence of pertussis by using DNA fingerprinting to characterize strains collected between 1949 and 1996. Two virulence factors, pertussis toxin and pertactin, exhibited polymorphism, and antibody responses to these proteins correlated with protection from disease. Furthermore, the polymorphism in pertussis toxin is restricted to a subunit that binds to the T cell receptor. It seems that the immune response generated to the vaccine strains may select for novel strains of the pathogen and that the crashes in diversity seen in the 1960s and 1980s may be explained by clonal expansion. Thus, vaccination has shifted the competitive balance among the strains, but it is not yet clear whether polymorphism directly affects vaccine efficacy or reemergence of disease. — CA

*Emerg. Infect. Dis.* **7**, Suppl. (June 2001).

CREDITS: WANG *ET AL.*, *ASTROPHYS. J.* 555, L99 (2001).