WEB WATCH

Mad scientists

With the recent furore over foot and mouth disease in Europe, bovine spongiform encephalopathy (BSE) has, for the moment, stepped out of the public eye. Tucked away on the internet, however, is the Official Mad Cow Disease Home Page, which claims to host over 7,431 articles on Creutzfeldt–Jakob disease (CJD), prions, BSE, scrapie and other transmissible spongiform encephalopathies.

What this site lacks in flashy graphics and design, it makes up for in the sheer volume of information — the news archives date back to March 1996, and the prion science archives to October of that year. New information is added at least once per week, from sources including international news agencies and newspapers as well as scientific journals.

We especially like the 'Best Links' page, which directs readers to sites such as databases, genomes, journals, meetings and contacts. There is also a comprehensive — albeit slightly daunting for the non-specialist — list of links to online tools. Government and public-interest sites are listed as well, although some links are of dubious quality.

In addition to these links, the site itself hosts a number of useful resources. These include an image gallery of three-dimensional prion structures, a graphics index, a tutorial on genome annotation and a curated database of all available prion and prion-like sequences. One criticism, though, is that the site is not very easy to navigate, and a site map would be useful to highlight the wealth of resources available.

Finally, the tantalisingly titled section on 'mad scientists' warrants a mention. Disappointingly, however, this is simply an eclectic bag of news snippets on a handful of researchers.

Alison Mitchell

PRIONS

A big jump across the species barrier

Yeast Sup35 self-propagates in a similar way to mammalian prions, transmitting the prion element [PSI$^+$], which confers heritable suppression of nonsense mutations. There is a robust species barrier between the yeasts *Saccharomyces cerevisiae* and *Candida albicans*, and prions from one species cannot 'infect' prions of the other species.

To examine the relationship between the primary structure of prions and their species specificity, Chien and Weissman constructed a chimeric (CHIM) protein using the first 39 amino acids of the *S. cerevisiae* prion domain (SC) and amino acids 40–140 of the *C. albicans* prion domain (CA). To their surprise, they found that their chimera was able to jump the species barrier, as transient overexpression of CHIM could induce the formation of [PSI$^+$] in yeast expressing SC, CA or CHIM. Conversely, SC, CA or CHIM could induce a [PSI$^+$]-like state in CHIM-expressing yeast.

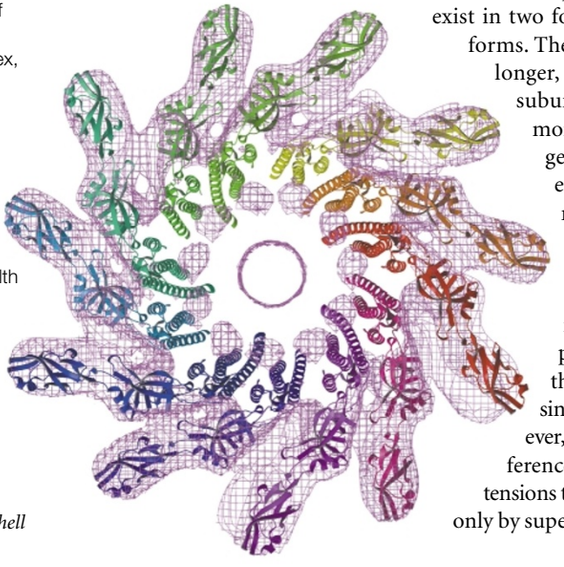
Remarkably, inducing the conversion of CHIM with either SC or CA gave rise to distinct prion strains — CHIM[SC] and CHIM[CA] — with different strain phenotypes *in vivo* and different fibre conformations *in vitro*. Second-generation fibres showed marked differences in seeding specificity: CHIM[SC] could seed only CHIM and SC but not CA, whereas CHIM[CA] could seed only CHIM and CA but not SC.

So it seems that the diversity of strain phenotypes might rely on the ability of a prion protein to adopt several self-propagating

MICROBIOLOGY

Flagellin shifts gear

The swimming of bacteria such as *Salmonella typhimurium* and *Escherichia coli* is driven by the rotation of flagella, no more than 0.25 μm in diameter but as much as 60 times that in length. The bacteria alternate between 'running' in a straight line and chaotic 'tumbling', while the rotary motor at the base of a flagellum changes from anticlockwise rotation to clockwise and back again. Reporting in *Nature*, Keiichi Namba and colleagues at the Protonic Nanomachine Project in Kyoto, Japan, have begun to work out the subtle atomic-level changes that couple these two events.



The bacterial flagellum consists over almost all of its length of a single protein, flagellin. Thousands of flagellin molecules form a hollow tube composed of 11 simple polymer threads, known as protofilaments. Electron microscopy of flagella has revealed that the protofilaments can exist in two forms, the L and R forms. The L form is slightly longer, with its flagellin subunits being 0.8 Å more elongated. A flagellum made up entirely of protofilaments of either type is straight and, although good for structural studies, it makes a poor propeller. Mixing the two forms in a single flagellum, however, means that the difference in lengths sets up tensions that can be resolved only by supercoiling the flagellum into a corkscrew shape.

When bacteria are swimming in a straight line, the flagella usually have nine L-type and two R-type protofilaments, producing a left-handed corkscrew. These flagella can bundle together to form a coordinated propulsion unit. When the flagellar motors reverse direction, a number of L-type protofilaments change to R-type protofilaments through a cooperative change in each flagellin molecule, right along the flagellum's length. Right-handed supercoiled flagella are produced, breaking up the flagellar bundles and leaving the individual flagella to push in different directions — this produces the tumbling motion. A very small change in flagellin's structure is thus at the heart of the bacterium's change in behaviour.

Proteins that form polymers pose a particular problem to structural studies; rather than forming well-ordered crystals, they tend to produce poorly ordered aggregates of their polymers. Consequently, Namba and colleagues studied a version of flagellin from *Salmonella* lacking 52 amino acids from its amino terminus and 44 amino acids from its carboxyl terminus. On solving its structure at 2.0-Å resolution, the authors found that the flagellin proteins were arranged as if single protofilaments were running throughout the crystals. This high-resolution crystal structure