the researchers took a closer look at this protein's activation profile during the development of individual anterior corner cell (aCC) motoneurons. As the researchers noted in the whole embryos, FRET signals from the A-probe were highly restricted in aCC cells. "When they're born and migrate and start generating axons, Cdc42 is silent," says Chiba. "Only towards the end of axonogenesis and the beginning of dendrogenesis does this molecule become activated for the first time." Notably, Cdc42 activity was also spatially restricted to the axon segment of the developing aCC neuron from which the dendrites emerge.

Overexpression of a constitutively active form of Cdc42 in aCC cells led to a variety of developmental defects, whereas overexpression of the wild-type protein had no apparent effect at all—providing additional confirmation of the primacy of specific activation over mere presence as a determinant of Cdc42 activity.

Chiba and Kamiyama believe such constructs could provide a generalizable strategy for tracking the activation of other signaling proteins *in vivo* and are currently developing FRET- and non-FRET-based activation bioprobes for other proteins involved in nervous system development. "If you do *in situ* hybridization in a tissue, you can see what genes are expressed," says Chiba. "But this kind of FRET-based bioimaging allows us to study the behavior of signaling proteins and monitor them at the level of protein-protein interactions."

Michael Eisenstein

RESEARCH PAPERS

Kamiyama, D. & Chiba, A. Endogenous activation patterns of Cdc42 GTPase within *Drosophila* embryos. *Science* **324**, 1338–1340 (2009).

new prion. Thus, Soto proposes that "the universe of possible prions is not restricted to what we know in nature…, and the sequence of the protein can accommodate many more prions that we [know of] today, and some of these could be potentially more virulent or more transmissible," analogous to today's situation with the influenza virus. But unlike with the flu, for which the new culprit mutant can be identified using existing technologies, protein-to-protein transmission complicates the study of prion disease. PMCA, however, is a powerful tool for this task: the original PMCA conditions can be used as a diagnostic assay to detect preformed prions in samples, and the extended PMCA is a model for studying the sporadic origin of prions.

The question of the molecular basis for this phenomenon still remains: "How can one single protein without changes in the amino acid sequence encode all the diversity that you have in prions? What are the differences between them, and how they produce the diseases? We are now studying this with natural prions and *de novo*–produced prions," says Soto.

So new insights into these confounding diseases are on the way, and PMCA is an adaptable tool for the task.

Irene Kaganman

RESEARCH PAPERS

Barria, M.A. *et al. De novo* generation of infectious prions *in vitro* produces a new disease phenotype. *PLoS Pathog.* **5**, e1000421 (2009).

Saborio, G.P. *et al*. Sensitive detection of pathological prion protein by cyclic amplification of protein misfolding. *Nature* **411**, 810–813 (2001).

NEWS IN BRIEF

PROTEOMICS

Defining RNA-binding protein preferences

RNA-binding preferences for only a few RNA-binding proteins (RBPs) have been determined, in part because existing methods are costly and laborious. Ray *et al.* describe a rapid approach, called RNAcompete, and use it to define RNA-binding specificities for nine RBPs. In this method, a diverse RNA pool is first generated; RNAs that bind to an RBP of interest are pulled down, fluorescently labeled and then analyzed via a microarray.

Ray, D. *et al. Nat. Biotechnol.* **27**, 667–670 (2009).

CHEMICAL BIOLOGY

Quantum dot biosynthesis

Quantum dots are widely used in imaging applications. The synthetic methods used to make CdSe quantum dots, however, are anything but environmentally friendly. Seeking a more benign synthetic approach, Cui *et al.* now report a method to biosynthesize quantum dots in yeast cells. They do this by carefully controlling the timing and duration of the incubation of the yeast with Na_2SeO_3 and $CdCl_2$ to generate CdSe quantum dots of various sizes with various fluorescence emission wavelengths.

Cui, R. *et al. Adv. Funct. Mater.* advance online publication (12 June 2009).

GENOMICS

Designing GWASs

Genome-wide association studies (GWASs) are very powerful methods for finding genetic variants that indicate risk for disease. Designing good GWASs, however, takes a lot of careful planning and usually a big budget. Spencer *et al.* describe a simulation method to assess the statistical power of different genotyping chips. Contrary to popular belief, they show that the chip with the highest coverage is not necessarily the best tool for the job.

Spencer, C.C.A. *et al. PLoS Genet.* **5**, e1000477 (2009).

BIOSENSORS

Detecting ozone

Although the stratospheric ozone layer crucially protects life on Earth from harmful ultraviolet rays, ground-level ozone is toxic. Garner *et al.* describe a small molecule–based, fluorescent turn-on probe for ozone, which can be used both as an atmospheric and a cell-based ozone sensor. This probe is highly selective for ozone and is not sensitive to the presence of other reactive oxygen species; it is a promising tool for better understanding the role of ozone in tissue damage.

Garner, A.L. *et al. Nat. Chem.* **1**, 316–321 (2009).

PROTEIN BIOCHEMISTRY

Enzymes for glycosphingolipid synthesis

Hancock *et al.* describe the generation of 'designer' enzymes for glycosphingolipid synthesis, using rational mutagenesis–based directed evolution and an enzyme-linked immunoassay (ELISA)–based screen to select glycosynthase mutants with improved catalytic activity. These enzymes could potentially be used to synthesize large quantities of pure glycosphingolipids for therapeutic applications.

Hancock, S.M *et al. Nat. Chem. Biol.* **5**, 508–514 (2009).