

## NEWS IN BRIEF

technical hurdle was to develop advanced imaging techniques; both groups developed custom-built three-dimensional confocal video microscopy systems allowing multicolor live-cell imaging at unprecedented resolution. “We can now clearly observe the tubular network structure of yeast Golgi cisternae, which we never imagined to see without the use of electron microscopy,” says Nakano. Both groups used GFP to label a *cis* Golgi resident protein and a red fluorescent protein variant to label a *trans* Golgi protein (or vice versa). They hypothesized that if proteins moving through the Golgi are transported by vesicles, then the green fluorescence marking an individual *cis* cisterna should be retained indefinitely. If cisternae mature from a *cis* state to a *trans* state, however, then the fluorescence should change from green to red as cisternae acquire new biochemical properties.

Both groups clearly observed that individual green *cis* cisternae changed color to red over a matter of minutes (Fig. 1). “The color change clearly ruled out the classic simple vesicular transport model,” explains Nakano. Glick was also surprised that the visual evidence for cisternal maturation was so clear-cut. “We had been concerned that Golgi cisternae might undergo frequent fusion and fission, and that these events would complicate the interpretation,” he says.

The success Glick and Nakano have had in answering a long-standing question in cell biology is also an excellent example of how working together rather than racing to compete for the same goal can provide fruitful results. “These papers will be scrutinized closely, so it was important to take the time to do the experiments right,” says Glick. “The fact that our two groups independently reached similar conclusions is reassuring and should also make the story more persuasive to others in the field.”

Allison Doerr

## RESEARCH PAPERS

Losev, E. *et al.* Golgi maturation visualized in living yeast. *Nature*; published online 14 May 2006.

Matsuura-Tokita, K. *et al.* Live imaging of yeast Golgi cisternal maturation. *Nature*; published online 14 May 2006.

which is something that DNA microarray experiments are not capable of doing,” explains Weissman.

This clever experimental design allowed Weissman, Newman and their colleagues to make global observations about the structure of biological noise in the cell. For example, proteins exhibiting very low noise included those involved in translation and protein degradation. Proteins with noisy expression included those involved in chromatin remodeling. Not surprisingly, some of the proteins with the most variable or noisiest expression were the ‘first responders’ to changing environmental conditions, such as those related to stress response and heat shock. Weissman remarks, “The implication is that this may be a way for cells to generate diversity in the phenotype even under one condition, so that if conditions change, there will be at least a subset of cells that will be better optimized to respond to that change.”

Allison Doerr

## RESEARCH PAPERS

Newman, J. R. S. *et al.* Single-cell proteomic analysis of *S. cerevisiae* reveals the architecture of biological noise. *Nature*; published online 14 May 2006.

## MICROARRAYS

## A robust small-molecule microarray platform for screening cell lysates

Bradner *et al.* present a process for the simplified construction of covalently linked small-molecule microarrays that present a diverse variety of natural and synthetic compounds. They subsequently show how the screening process can be simplified by using whole lysates from cells in which the protein of interest is expressed with an epitope tag or as a fluorescent chimera.

Bradner, J.E. *et al.* *Chem. Biol.* **13**, 495–504 (2006).

## BIOINFORMATICS

## Computational redesign of endonuclease DNA binding and cleavage specificity

Working with a computational strategy that allows atomic-level modeling of protein-DNA interfaces, Ashworth *et al.* designed a variant of the homing endonuclease I-*Mso*I with altered target preference. This modified enzyme displayed 10,000-fold enhanced binding and cleavage of an alternate site, with target-discrimination capabilities that are equivalent to the wild-type enzyme.

Ashworth, J. *et al.* *Nature* **441**, 656–659 (2006).

## PROTEOMICS

## A pharmacological map of the PI3-K family defines a role for p110 in insulin signaling

The 15 kinases of the phosphoinositide 3-kinase (PI3-K) family are recognized as important drug targets, but the physiological roles of individual kinase isoforms are poorly understood. Knight *et al.* screened a large library of PI3-K inhibitors, revealing details about target specificity, which could provide valuable insights into isoform-specific function and assist in future drug-design efforts.

Knight, Z.A. *et al.* *Cell* **125**, 1–15 (2006).

## IMAGING AND VISUALIZATION

## Virtual histology of transgenic mouse embryos for high-throughput phenotyping

Magnetic resonance microscopy (MRM) is a powerful tool for embryological imaging, but it may not be a practical option for large-scale screening. Johnson *et al.* present a less expensive alternative for high-throughput work, using X-ray microscopic computed tomography (microCT) with osmium tetroxide-stained mid-gestation embryos to achieve rapid, high-resolution imaging.

Johnson, J.T. *et al.* *PLoS Genet.* **2**, e61 (2006).

## GENOMICS

## Regulatory blueprint for a chordate embryo

Previous *in situ* hybridization studies have identified 76 genes regulating embryogenesis in the tunicate *Ciona intestinalis*. By analyzing gene-expression changes in response to disruption of these genes, Imai *et al.* assembled a detailed map of the genetic circuits underlying the formation of various organs and tissues, information that could yield important insights into chordate evolution.

Imai, K.S. *et al.* *Science* **312**, 1183–1187 (2006).