

astonishing: you have a structure self-assembled from one component less than 1,000 daltons in molecular weight; this molecule can be well characterized, and the resulting structure achieves many functions without stacking together different components as with other multifunctional platforms,” he says.

Porphysomes could be used to switch from photoacoustic imaging to fluorescence imaging. For instance, when the researchers modified the particles to contain 1% folate and applied them to folate receptor-expressing cells, the fluorescence signal only ‘came on’ when the particles had been endocytosed and presumably broken apart within the endosome. *In vivo*, upon intradermal injection of porphysomes into rats, the photoacoustic signal could be used to monitor the local lymphatic vasculature and the draining lymph node, and in a tumor model, the particles could be monitored as they accumulated in the tumor and their fluorescence quenched.

Finally, porphysomes are enzyme-degradable and could therefore turn out to be biodegradable also *in vivo*. “We got the components from nature,” says Zheng. “We got the porphyrin from algae that you can actually find in a health-food store.” It should be noted that the algal porphyrin is modified in the laboratory, and that long-term toxicity of porphysomes has still to be tested, but rats could tolerate very high intravenous doses over the short term with no apparent ill-effects.

It is an attractive idea that the solution to a knotty problem lies in simplicity. To make multifunctional particles with the capacity for nontoxic drug or contrast-agent delivery, simplicity may indeed be the key.

Natalie de Souza

RESEARCH PAPERS

Lovell, J.F. *et al.* Porphysome nanovesicles generated by porphyrin bilayers for use as multimodal biophotonic contrast agents. *Nat. Mater.* **10**, 324–332 (2011).

Although Horn acknowledges that the datasets with loss of fitness in all four conditions are more robust, he sees the differentiation-specific genes also as potential drug targets. “A drug could trigger the cells in the patient to differentiate,” he says, “and in the process they lose their glycoprotein coat and become subject to complement mediated lysis.”

It goes without saying that all these results require experimental follow-up. Horn has released all the screening data on TriTrypDB, a site for kinetoplastid genomics resources. His team is now doing selective drug-resistance screens to get at the pathogen-specific uptake and metabolism of certain compounds.

“We need more resources to move the field forward more rapidly,” Horn says. Helpful resources would include a collection of defined RNAi lines to do gain-of-function screens and more precise follow-up.

Horn also points out that the principle behind RIT-seq could be applied to other parasites as well, as long as they have an RNAi machinery.

For the time being, the rich data resource Horn’s team created will help with drug target triage and assist in the first steps toward more effective disease treatment. Go to <http://www.youtube.com/watch?v=WhdYbrv3YC5> to see for yourself how sorely treatment is needed.

Nicole Rusk

RESEARCH PAPERS

Alsford, S. *et al.* High-throughput phenotyping using parallel sequencing of RNA interference targets in the African trypanosome. *Genome Res.* advance online publication (1 March 2011).

GENETICS

Temperature-sensitive yeast mutants

Li *et al.* present a collection of temperature-sensitive mutants of almost half of the essential genes in yeast, in a genetic background appropriate for interaction screening using the synthetic genetic array method. Barcoding of the collection permits chemical-genetic suppression screening and combination with fluorescent markers of subcellular structures enables high-content screening of double-mutant phenotypes in single cells. Li, Z. *et al.* *Nat. Biotechnol.* **29**, 361–367 (2011).

MASS SPECTROMETRY

HCD without a dedicated collision cell

In proteomics applications, especially for *de novo* sequencing and identifying protein modifications, peptides can be efficiently fragmented by tandem mass spectrometry via high-energy collision-induced dissociation (HCD) involving a specialized collision cell. McAlister *et al.* now show that HCD can be performed in the ion injection pathway of any mass spectrometer with a common atmospheric inlet, without a dedicated collision cell. McAlister, G.C. *et al.* *Mol. Cell. Proteomics* advance online publication (10 March 2011).

GENOMICS

GROMIT looks at the regulatory genome

To find regulatory elements in the mouse genome, Ruf *et al.* developed genome regulatory organization mapping with integrated transposons (GROMIT), a strategy that uses the Sleeping Beauty transposon containing a *lacZ* reporter gene driven by a minimal promoter that responds to nearby enhancers. Following the expression patterns of the reporters in single-integrant mouse lines, they found transcriptional activity all over the chromosomes. Currently available lines cover about 10% of the mouse genome.

Ruf, S. *et al.* *Nat. Genet.* **43**, 379–386 (2011).

CHEMICAL BIOLOGY

Protein control with a photoactivatable split intein

Binschik *et al.* introduce a photoactivatable split-intein system for studying protein function in the living cell. Attaching one half of the split intein to the pathogenic protein staphylocoagulase modulated its binding to prothrombin in human blood plasma. Upon light activation, a bulky caging group is cleaved off the other half of the split intein, facilitating the splicing reaction, and resulting in the cleavage of staphylocoagulase and the restoration of its activity.

Binschik, J. *et al.* *Angew. Chem. Int. Edn.* **50**, 3249–3252 (2011).

NEUROSCIENCE

Addressing errors in patch clamping

The cell-attached patch clamp configuration is useful for investigating the functional properties of voltage-activated ion channels without substantially disturbing the rest of the cell. Williams and Wozny carefully examine the errors associated with such measurements and introduce simple correction procedures; in particular they found that the amplitude and kinetics of ion-channel activity can be distorted by transmembrane voltage changes associated with current flow.

Williams, S.R. & Wozny, C. *Nat. Commun.* **2**, 242 (2011).