TOOLS IN BRIEF

GENETICS

A genome-wide TALEN resource

Genome editing using targeted nucleases involves cleaving DNA at a desired site in the genome and then harnessing cellular repair machineries to either introduce mutations or to add exogenous sequence. Transcription activator–like effector nucleases (TALENs) are attractive tools for this purpose. Kim *et al.* now report a collection of TALENs targeting all protein-coding genes in the human genome. They use an algorithm to select target sites that are 32–40 base pairs long, that do not have related sites elsewhere in the genome and that occur toward 5′ ends of genes. They assembled almost 19,000 TALEN pairs using a Golden Gate cloning approach. Of the 126 TALEN pairs tested, 124 generated mutations at the desired site in HEK293 cells. Plasmids required for TALEN assembly are available to the research community.

Kim, Y. *et al. Nat. Biotechnol.* **31**, 251–258 (2013).

MOLECULAR ENGINEERING

'Self' peptides for enhanced delivery

An unsolved problem in the tumor targeting and imaging field is that the targeting and imaging agents are subject to being engulfed by macrophages and therefore do not reach their molecular targets. Rodriguez *et al.* now report a synthetic 'self' peptide that binds to macrophages and inhibits the clearance of a particle to which the self peptide is attached. As a marker of 'self' (in mice), the researchers chose the ubiquitously expressed CD47 membrane glycoprotein. They designed a minimal synthetic peptide from CD47 and showed that by attaching it to an imaging agent it allowed enhanced *in vivo* tumor imaging in mice. The researchers speculate that additional self peptides could be discovered or designed to allow enhanced tumor imaging and drug delivery.

Rodriguez, P.L. *et al. Science* **339**, 971–975 (2013).

SENSORS AND PROBES

Protein degradation sensors

The accumulation of misfolded proteins in a cell or organism can be catastrophic. Endoplasmic reticulum–associated degradation (ERAD) is a constitutive process that identifies misfolded proteins in the ER and shuttles them to the cytosol, where they are degraded by the proteasome. Much, however, remains to be learned about the ERAD machinery and its function. Grotzke *et al.* simplify the task of studying this complex pathway by developing fluorescent sensors that act as ERAD substrates. The sensors are versions of the Venus fluorescent protein that only become fluorescent after they have been first glycosylated in the ER and later deglycosylated in the cytosol through the ERAD pathway. These proteins can also be fused to additional ERAD substrates to interrogate substrate-specific pathways. Grotzke *et al.* used the tools in a genome-wide short interfering RNA screen to identify ERAD factors.

Grotzke, J.E. *et al. Proc. Natl. Acad. Sci. USA* **110**, 3393–3398 (2013).

SYNTHETIC BIOLOGY

Logic and memory integrated in a synthetic circuit

One of the central goals in synthetic biology is to develop gene circuits that can be programmed to replicate cellular networks. Desired features in such circuits are logic gates that can easily be programmed and maintain memory so that the cellular states produced by the logic gates are retained over time. Siuti *et al.* used two inducible recombinases, a promoter and a terminator flanked by recognition sites for the recombinases and GFP as an output signal to create 16 Boolean logic functions. They arranged the regulatory elements in the desired orientation for a given logic gate using Gibson assembly and showed that cells maintained stable output memory for many generations after the input was withdrawn. As an application for a higher-order network the researchers built a digital-to-analog converter that allows cells to translate a digital input signal, activating the recombinases, to stable analog gene expression output.

Siuti, P. *et al. Nat. Biotechnol.* advance online publication (10 February 2013).