Weigh station for biological particles

Nanocantilevers determine the mass of small particles by measuring changes in the cantilever's resonance frequency caused by particle binding. For analytes in vacuum, resolution is on the order of zeptograms, but in aqueous solution it is much worse because of the effects of viscosity. Manalis and colleagues have developed a device for weighing particles in aqueous solution that achieves subfemtogram resolution—about a million times lower than that of a quartz crystal microbalance. Instead of binding to the outside of the resonator, particles flow through the resonator in a microfluidic channel. The cantilever is suspended in a vacuum to maximize sensitivity. Particles can be weighed by capturing them with affinity reagents immobilized in the channel, and even unbound particles can be measured as they reach the cantilever's apex, where the frequency shift is greatest. The dynamic range of the device is higher than seven orders of magnitude. The authors demonstrate mass determination of protein monolayers, nanoparticles and bacterial cells. Future versions will have microfluidic channels that are large enough to accommodate eukaryotic cells. (*Nature* **446**, 1066–1069, 2007) *KA*

T-cell receptor domain combats toxic shock

Many pathogenic bacteria produce superantigens that bind to variable regions (Vβ) of T-cell receptors with low affinity. Such binding can trigger massive inflammatory cytokine secretion, potentially resulting in toxic shock syndrome and even death. Buonpane *et al.* have engineered high-affinity, soluble Vβ domains for use as potential neutralizing agents of one such superantigen, staphylococcal enterotoxin B (SEB), a primary cause of staphylococcal toxic shock. Generating five successive mutagenesis libraries of the SEB:Vβ interface, they obtained Vβ domains that bind SEB with high affinity. The final generation shows a three million–fold increase relative to the wild-type SEB-Vβ interaction, with a clear correlation between affinity and neutralizing potential *in vitro* and in a rabbit model of toxic shock syndrome. Whereas rabbits administered SEB develop fever and die, those treated with Vβ, either before or after the toxin, exhibit no elevated temperature and survive. In a second rabbit model where SEB is slowly delivered in a manner that more closely mimics staphylococcal infection, rabbits treated with Vβ survive, whereas untreated rabbits die. Vβ agents have been shown to be capable of cross-neutralization, and given that bacterial infections typically involve multiple toxins that require neutralization, ultimately it may be possible to tailor Vβ therapy to treat toxins identified in a specific patient's serum. (*Nat. Med.* **13**, 725–729, 2007) *TB*

Enhanced iron acquisition in rice

The low availability of iron in alkaline soils—and not its absence *per se*—is often a major limitation for plant growth, especially for crops such as rice that lack the ability to induce ferric iron chelate reductase activity for conversion of Fe^{3+} to the easily absorbable Fe^{2+} ion. Ishimaru *et al.* transform rice to express a yeast Fe^{3+} chelate-reductase, previously selected for enhanced activity as high pH, under the regulation of the promoter of a gene encoding a rice Fe^{2+} transporter. This confers iron-responsive transgene regulation in the root epidermis. An increase in iron uptake correlates with an approximately eightfold increase in grain yield for plants grown in calcareous soil. Rather disappointingly, this is not accompanied by an increase in the iron content of the grain, although better insight into iron transport may address the need for biofortification with this essential nutrient. Stacking the capacity for inducible Fe^{3+} reduction on other approaches to improve iron availability, such as phytosiderophore synthesis, might further enhance the potential to expand rice cultivation to marginal soils. (*Proc. Natl. Acad. Sci. USA* **104**, 7373–7378, 2007) *PH*

Modeling leukemia

Animal models of leukemia, although easily manipulated and instructive, cannot provide information on the type of cells that initiate the disease in humans. Now Barabé *et al.* have described a mouse model that recapitulates the human disorder, providing insights into disease pathogenesis. They accomplish this by transplanting into immunodeficient mice an enriched population of stem and progenitor cells, isolated from human umbilical cord blood, that have been transfected with mixed-lineage leukemia genes found in humans with acute myeloid and acute lymphoid leukemia. The majority of the transplanted mice develop leukemia with a short latency, and have cell surface phenotypes and the tissue infiltration patterns resembling those found in human disease carrying the same mixed-lineage leukemia gene. By doing serial transplantations and comparing the clonal properties of leukemia cells in primary and secondary transplants, the researchers find evidence that the initiating cells evolved from a primitive cell (that is, with the germline configuration of IgH genes), the likely target of transformation, to cells with rearranged genes. A better understanding of the cellular and molecular properties of leukemia-initiating cells will help inform therapies for people suffering from this disease. (*Science* **316,** 600–604, 2007) *LD*

ChIP-MPSS mapping of histone modifications

Histone modifications regulate gene expression and genome function. The ChIP-on-chip technique, a combination of chromatin immunoprecipitation (ChIP) and DNA-microarray (chip) analysis, enables genome-wide scale mapping of histone modifications. Because ChIP-on-chip requires large sets of arrays and is prone to potential bias, alternative technologies are desired. Zhao and colleagues map histone modifications by directly sequencing ChIP DNA from mononucleosome preparations with the Solexa (now Illumina; San Diego) 1G Genome Analyzer. After a one-step adaptor ligation and 17 PCR cycles the ChIP DNA is sequenced by massive parallel signature sequencing on arrays. One sequencing run can generate 20 million sequence tags of up to 36 bp each. The majority of these tags can be mapped to the human genome and the number of tags is proportional to the modification level of a particular nucleosome. After generating single-nucleosome resolution maps for 20 histone lysine and arginine methylations, RNA polymerase II and two other proteins, the authors correlate their localization patterns with gene expression profiles from human resting $CD4^+$ T cells. Whereas monomethylations of H2BK5, H3K9, H3K27, H3K79 and H4K20 are associated with expressed genes, trimethylations of H3K9, H3K27 and H3K79 correlate with inactive genes. This study shows that technologies with short sequencing reads can substantially speed up mapping proteins and their modifications to complete genomes. (*Cell* **129,** 823–837, 2007) *JWT*

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