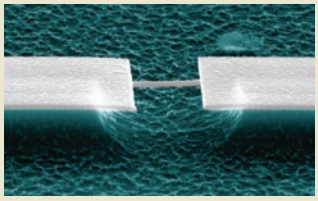
Single-molecule mass spectrometry?



Mass spectrometry (MS) measures the mass-to-charge ratio of sample molecules in a three-step process (analyte ionization, separation and detection) that limits sensitivity and restricts analysis to molecules that can be efficiently ionized. Naik *et al.* present an MS technology capable of measuring the mass of sample molecules during the detection step with single-molecule sensitivity, which ultimately could remove the necessity for ionization. Molecules are detected when they adsorb to the surface of a nanomechanical system that oscillates at ultrahigh frequencies. The resonance frequency of nanomechanical systems depends critically on the mass of the system and changes detectably upon binding of a single molecule. The exact change of the frequency depends on the mass of the binding molecule. Using gold nanoparticles, bovine serum albumin (BSA) and β-amylase as model analytes, the authors accurately determine molecular masses and detect multimerization of BSA. Electrospray ionization strips the analytes from solvent and transports them to the surface of a single sensor, but arrays of detection surfaces and improved mass transport technologies might allow highly sensitive, massively-parallel mass spectrometers on a chip, each with single-molecule resolution. (*Nat. Nanotechnol.* **4**, 445–450, 2009) *ME*

Anticancer miRNA therapy

Regulatory RNAs are being exploited as potential therapeutics in various conditions, often through antisense suppression of micro (mi) RNAs. But in tumors, some miRNAs normally expressed at high levels are themselves repressed. This suggested to Kota *et al.* that reintroduction of miR26a, an miRNA expressed in normal tissues but repressed in liver tumors, might be exploited as an anticancer therapy. They engineered an adeno-associated viral vector to express miR26a and green fluorescent protein and introduced it into a mouse model of liver cancer. After injecting the vector into the tail vein of these mice, the authors found high levels of miR26a in the liver, and, by fluorescence microscopy, they could see that >90% of the hepatocytes were transformed. Finally, in mice given the virus seven weeks after liver cancer had been induced, eight of ten animals had small or no tumors, whereas six of eight control mice had fulminant disease. This is one of the first demonstrations that an exogenously administered miRNA can ameliorate an oncogene-driven cancer and suggests that other miRNAs with similar therapeutic potential might be possible in other cancers. (*Cell* **137**, 1005–1017, 2009) *LD*

Flatworm genomes for schistosomiasis

Schistosoma japonicum and *Schistosoma mansoni* are two of the three principal flatworms responsible for schistosomiasis, a neglected tropical disease that ranks with malaria and tuberculosis as a major source of morbidity in many developing countries. Zhou *et al.* and Berriman *et al.* report draft genomic sequences of both species, analysis of which suggests new approaches to treat and eradicate this debilitating disease. At 397 Mbp and 363 Mbp, respectively, the genomes of *S. japonicum* and *S. mansoni* are >15 times the size of the protozoan responsible for malaria and are the first genomic sequences of members of the Lophotrochozoa, a large taxon comprising ~50% of all animal phyla. As no vaccine and only a single drug, praziquantel, are currently available to manage schistosomiasis, it is hoped that the estimated 13,469 and 11,809 genes in the two genomes hold the key to novel, more efficacious therapies. For instance, members of the expanded gene families encoding proteases or enabling the parasites' sophisticated neurosensory systems, or the flukes' dependence on human hosts for sterols and free fatty acids might be exploited as an Achilles' heel in drug-development efforts. Berriman *et al.* suggest that 66 currently marketed drugs might be repurposed to target 26 gene products in *S. mansoni*. (*Nature* **460**, 345–351, 2009; *Nature* **460**, 352–358, 2009) *PH*

Written by Laura De Francesco, Markus Elsner, Peter Hare & Craig Mak

Web 2.0 genome browsing

Breathtaking innovation has fueled genome-scale data acquisition. But improvements to one of the main tools for visualizing these data—the genome browser—have lagged behind. To address this gap, Skinner *et al.* present JBrowse, a next-generation genome browser uniquely defined by its ability to offload much of the computation-intensive work of data visualization to a user's web browser. As with existing genome browsers, JBrowse displays a portion of a genome annotated with sequence features such as genes, transcription factor binding sites or epigenetic marks. But unlike available browsers, where all or most of the computation occurs on a remote web server, JBrowse obtains specially processed data from the internet and graphically displays it using what is essentially a self-contained program that is loaded into a user's web browser on the fly from a web page. JBrowse (http://jbrowse.org/) is open source, free for academic and commercial use, and has been tested with popular web browsers. JBrowse enables intriguing future applications, including embedded genome browser widgets (think of a Google map embedded on a non-Google web page) or genome data 'mashups' (think of real estate prices overlaid on a street map). (*Genome Res.*, published online July 1, 2009; doi:10.1101/gr.094607.109) *CM*

Complexity in DNA binding

DNA binding transcription factors recognize a specific sequence motif—at least that's the dogma. But data reported by Bulyk and colleagues suggest that many transcription factors bind 'secondary motifs' *in vitro*. These motifs were identified using universal protein binding microarrays (e.g., see *Nat. Biotechnol.*, **24**, 1429–1435, 2006) to analyze 104 mouse transcription factors. The microarrays were synthesized to contain DNA oligonucleotides representing every possible contiguous and gapped 8-mer sequence spanning up to 12 total bases embedded within 60 nt oligos (>41,000 probes on the array). These single-stranded arrays were then biochemically converted to double-stranded DNA arrays, which provided substrates for transcription factor binding. Glutathione *S*-transferase fusion proteins were incubated on the array and then imaged using fluorescence-conjugated antibodies, thereby identifying the 8-mer sequences bound by the protein. In total, about half of the transcription factors were observed to bind 'secondary motifs' that differed substantially from the primary motifs of that factor. Computational analyses and comparison to *in vivo* binding data suggested that, for at least some factors, these secondary motifs represent novel biologically relevant DNA binding potential, although the functional consequences of this binding remain to be explored. (*Science*, **324**, 1720–1723, 2009) *CM*