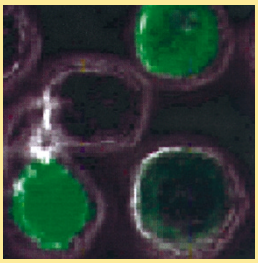
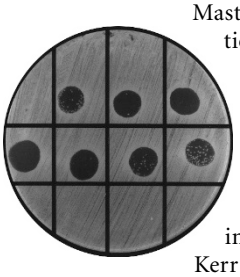


On page 40, Faria *et al.* establish the mechanism of action of N3′-P5′ phosphoramidate (NP) oligonucleotides, which belong to a new generation of antisense reagents that have considerable promise as therapeutic reagents, as shown in a number of *in vivo* studies. Their extremely high nuclease resistance and tight binding to single-stranded RNA initially piqued the interest of researchers; however, whether they exert their effect directly on mRNA or by interacting with other cellular components, as has been shown for some other types of therapeutic antisense reagents, was until now unclear. Faria *et al.* established a reporter system to examine whether the oligo acted by binding to its target sequence upstream of the luciferase gene. In both cell culture and skeletal muscles *in vivo*, the oligos acted by steric blockage of translation initiation, and not by inducing RNase H, another common mechanism of antisense reagents (see also p. 17). *ND*

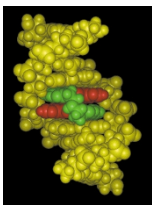
Got milk?



Mastitis, a kind of infection of mammary tissue, costs the US dairy industry billions annually, and extracts an uncalculable cost in animal suffering. On page 66, Kerr *et al.* demonstrate a possible biotechnology solution: transgenic mice that secrete in their own milk a potent antibacterial protein, lysostaphin, that targets one of the main culprits, *Staphylococcus* sp. They introduced a pair of mutations in the bacterial lysostaphin gene that conferred staphylolytic activity, and fused it to part of the ovine β-lactoglobulin gene to mediate secretion into milk. Transgenic mice expressing the construct proved highly resistant to *S. aureus* infection, and were apparently otherwise unaffected. *JJ*

This Month in Nature Biotechnology *written by Natalie DeWitt, Judy Jamison, and Meeghan Sinclair.*

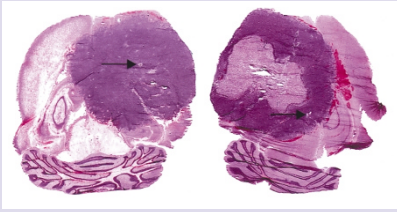
SNP detection made simpler?



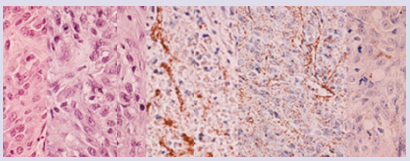
High-throughput technologies for detecting SNPs require knowledge of sequence information, and alternatives for scanning without such information rely on cumbersome, gel-based methods. On page 51, Nakatani *et al.* provide an alternative. They have isolated small molecules called dimeric naphthyridines that bind specifically to G•G mismatches. By coupling the ligand to a sensor chip for surface plasmon resonance, they could detect DNA containing G•G mismatches from PCR products amplified from real biological samples. The chemistry described in the paper could provide a starting point for development of related ligands that bind to other mismatches, and development of simple and sensitive chip-based SNP detection methods (see also p. 18). *ND*

Silent genes find a voice

Of the many thousands of genes encoding proteins of unknown function, the most enigmatic are the "silent" ones—those that exhibit no detectable phenotype when deleted from the genome. On page 45, Raamsdonk *et al.* show that, at least in yeast, gene function can be accurately predicted by examining the levels of various known metabolites. Using sophisticated statistical methods and NMR for comprehensive analysis of metabolite concentrations, the authors showed that, in principle, the function of silent genes can be revealed by comparing the metabolic profile of a yeast strain deleted for a silent gene to the profiles of deletion strains with known cellular roles. *MS*



In this issue two groups, Read *et al.* (see p. 29) and Joki *et al.* (see p. 35) describe a strategy for sustained delivery of the anti-angiogenic agent, endostatin, to tumors. Both groups engineered cells to express endostatin and then encapsulated them in sodium alginate, forming beads, an arrangement that promotes exchange of nutrients and oxygen to the cells, and protects them from tissue rejection. Both groups showed that the beads reduced tumor growth *in vivo*, using animal models of gliomas, a highly vascularized and invasive form of brain tumor. Read *et al.* implanted beads and tumor cells intracranially in rats, and Joki *et al.* implanted beads next to existing tumors growing under the skin of mice. Both groups subsequently observed reduced tumor growth, large areas of necrosis, and apoptosis in the endostatin-treated tumors. Given that continuous delivery may be key to the antitumor efficacy of endostatin, such cell-based approaches could hold promise for cancer therapy (see also p. 20). *MS*



Technical Reports

Phage display of antibody libraries is an undeniably powerful technique for isolating highly specific antibodies. However, in the most widely used systems only a small percentage of the phage population carries an antibody, so the libraries are large and unwieldy to screen. On page 75, Rondot *et al.* describe a new helper phage system that boosts the number of single-chain antibody fragments (scFv) presented on the filamentous bacteriophage by more than two orders of magnitude and show that it significantly increases the number of antigen hits from a given library. *MS*

On page 78, Zhou *et al.* describe a technique for scoring loss of heterozygosity in tumors. They used fluorescent molecular beacons and "digital PCR" to detect SNP loci for which the patient was heterozygous, and applied likelihood techniques to ask whether the markers were lost through allelic loss in tumors of 70 patients. The technique is reproducible enough to allow correlation of chromosome loss with an important biological property of tumors—vascular invasion. *ND*