izing specifically to the other via their complementary DNA sequences.

After confirming that the two dendrimers were, in fact, capable of hybridizing to each other, Baker's group tested to see whether the hybridized units integrated the functionality of both folate and fluorescein. The folate receptor is commonly overexpressed on the surface of human tumor cells; working with epithelial carcinoma cells, the researchers demonstrated that these linked dendrimers successfuly bound the receptor and were internalized and that fluorescein was clearly visible within the treated cells.

Although this *in vitro* data is promising, Baker is already looking ahead to the true test—therapeutic studies in animals. "We've been able to accomplish this in animals with a single polymer agent, and we saw specific targeting from just injecting the material into the bloodstream. So we'd like to see whether or not we could get the same effect in animals using these cluster agents."

Although this work was funded by the National Cancer Institute's Unconventional Innovations Program and was initially conceived as a system for the targeting of chemotherapeutic agents, Baker and his colleagues recognize that the system could be applicable to a number of other biomedical applications. "There are lots of other things we could address with the technology, in terms of delivering specific molecules to cells," he says. "For example, one important application is as a delivery platform for siRNA. This could facilitate an entire new field of therapeutics."

Large-scale development of this technology has been limited somewhat by the extremely high price of PAMAM polymers in bulk. Nonetheless, Baker anticipates that more opportunities will present themselves as their strategy catches on, and he adds, "I think there are a lot of companies that see the potential of delivering drugs this way."

Michael Eisenstein

RESEARCH PAPERS

Choi, Y. *et al.* Synthesis and functional evaluation of DNA-assembled polyamidoamine dendrimer clusters for cancer cell-specific targeting. *Chem. Biol.* **12**, 35–43 (2005).

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about the mechanism: "Longer is probably better because you enter the pathway at an earlier stage. There is evidence for Dicer association with RISC, so it is possible that Dicer processing and delivery to RISC underlies the enhanced potency of the longer RNAs." As a consequence, the performance of a suboptimal 21-mer can be substantially improved by placing the core sequence in a longer context.

Despite these positive results, both Rossi and Cleary acknowledge that longer oligos per se are not the magic bullet; although they are better than 21-mers, some still silence relatively poorly, so choosing the right sequence remains important. Both groups are currently working on attaining better sequence prediction and optimal Dicer recognition. A combination of both will most likely ensure efficient and lasting knockdown, making frustratingly inefficient siRNAs a thing of the past.

Nicole Rusk

RESEARCH PAPERS

Kim, D.H. *et al*. Synthetic dsRNA Dicer substrates enhance RNAi potency and efficacy. *Nat. Biotechnol.* **23**, 222–226 (2005).

Siolas, D. *et al*. Synthetic shRNAs as potent RNAi triggers. *Nat. Biotechnol.* **23**, 227–231 (2005).

NEWS IN BRIEF

IMAGING AND VISUALIZATION

Synthesis of water-dispersible, fluorescent, radio-opaque and paramagnetic CdS:Mn/ZnS quantum dots: a multifunctional probe for bioimaging

Santra *et al.* introduce a new class of stable, *in vivo*–friendly quantum dots (QDs), which, besides generating stable fluorescence, are also radio-opaque and paramagnetic, enabling detection by a variety of scanning methodologies and thus opening up new possibilities for noninvasive bioimaging.

Santra, S. *et al. J. Am. Chem. Soc.*, published online 21 January 2005.

DNA CLONING AND AMPLIFICATION

MAGIC, an *in vivo* genetic method for the rapid construction of recombinant DNA molecules

The mating-assisted genetically integrated cloning (MAGIC) system combines bacterial mating, *in vivo* site-specific endonuclease cleavage and homologous recombination to effect the transfer of DNA fragments between a donor vector in one bacterial strain and a recipient vector in a different strain, simplifying the construction of recombinant DNA libraries.

Li, M.Z. & Elledge, S.J. *Nat. Genet.*, published online 30 January 2005.

CHEMINFORMATICS

Metabolizing enzyme toxicology assay chip (MetaChip) for high-throughput microscale toxicity analyses

There is a need for *in vitro* assays that can identify toxic effects resulting from metabolic processing of drugs. Lee *et al.* introduce the MetaChip, a high-throughput system for such assays. An array of sol-gel–encapsulated cytochrome P450 enzymes is exposed to compounds of interest, and then is apposed against a monolayer of cultured cells, allowing direct assessment of toxicity.

Lee, M.-Y. *et al. Proc. Natl. Acad. Sci. USA* **102**, 983–987 (2005).

MICROARRAYS

Biosynthetic labeling of RNA with uracil phosphoribosyltransferase allows cell-specific microarray analysis of mRNA synthesis and decay

Cleary *et al.* introduce a microarray strategy designed to directly monitor changes in the production and degradation of mRNA over a set period of time. By tracking incorporation of a tagged uracil analog in newly synthesized transcripts, one can determine the extent to which shifts in mRNA abundance result from changes in rate of synthesis or transcript turnover.

Cleary, M.D. *et al. Nat. Biotechnol.*, published online 30 January 2005.

VIROLOGY

Human immunodeficiency virus type 1 vectors with alphavirus envelope glycoproteins produced from stable packaging cells

The Env glycoprotein is an essential determinant of host range for the human immunodeficiency virus (HIV); by incorporating Env variants, one can generate HIV-derived vectors capable of targeting both human and animal cells. Strang *et al.* have applied a stable HIV-1 packaging system, STAR, to generate alphavirus-pseudotyped HIV particles with considerably broadened tropism.

Strang, B.L. *et al*. *J. Virol.* **79**, 1765–1771 (2005).