and binds to the CAG-CAG triad. The 2-amino-1,8-naphthyridine moiety was designed to present hydrogen bonds complementary to guanine, and 8-azaquinolone to present hydrogen bonds complementary to adenine; the two groups are connected by a short, flexible linker. Solution of the NMR structure of the CAG-CAG triad revealed that two molecules of NA intercalate into the DNA helix, presenting hydrogen bonds to correct the A-A mismatch yet disrupting the C–G pair, causing the two cytidine nucleotides to 'flip' to the outside of the helix (**Fig. 1**, center and right).

The researchers used NA to create a surface plasmon resonance (SPR) biosensor that was sensitive to $(CAG)_n$ repeat length. "A longer $(CAG)_n$ repeat sequence bound to immobilized NA on the sensor more efficiently than the shorter $(CAG)_n$ repeat, and so we could see the difference in binding affinity by the SPR signal intensity," reports Kazuhiko Nakatani, principal investigator of this study. The NA-SPR sensor could be calibrated and used to determine $(CAG)_n$ repeat lengths, and therefore the severity of the disease state.

In addition to diagnosing $(CAG)_n$ repeat disorders, the discovery of NA may be an important step toward understanding the mechanism of trinucleotide repeat pathogenesis, and potentially, a cure. "One therapy may be to use NA to stop the translation of the $(CAG)_n$ repeat to the protein," says Nakatani. Nakatani and other researchers in this area are certainly hopeful that the discovery of new small-molecule ligands may one day open the door to effective therapies for this and other trinucleotide repeat expansion disorders.

Allison Doerr

RESEARCH PAPERS

Nakatani, K. *et al.* Small-molecule ligand induces nucleotide flipping in $(CAG)_n$ trinucleotide repeats. *Nat. Chem. Biol.* **1**, 39–43 (2005).

remains a promising breakthrough, both for transplantation work and for the generation of disease-specific cells for research purposes.

Schatten points out that newly passed Korean legislation, which allows but closely regulates therapeutic stem cell cloning, has been a tremendous asset: "As an American sitting in Pennsylvania, one of a handful of states that still makes human embryonic stem cell derivation a criminal felony, I would have to say that more important than having the scientific skills, more important than having the research resources, is having a clear and enabling institutional state and national policy."

Indeed, these are trying times for American stem cell researchers, but Schatten remains positive, preferring instead to focus on gains like the recent Congressional vote to expand therapeutic stem cell work—even in the face of a veto threat. Above all, he is grateful for the chance to collaborate on this work with his international partners: "Without them, this type of research might have been delayed for decades… I just think we all owe them an immense debt of gratitude."

Michael Eisenstein

RESEARCH PAPERS

Hwang, W.S. *et al.* Patient-specific embryonic stem cells derived from human SCNT blastocysts. *Science*; published online 19 May 2005.

Hwang, W.S. *et al.* Evidence of a pluripotent human embryonic stem cell line derived from a cloned blastocyst. *Science* **303**, 1669–1674 (2004).

NEWS IN BRIEF

CHEMICAL TOOLS

Phosphorylation-driven protein-protein interactions: a protein kinase sensing system

Fluorescent probes are promising tools for the monitoring of kinase activity, but there remains a need for generalized strategies that can be applied to generate indicators for virtually any specific kinase. Wang and Lawrence describe such a strategy for probe design, an approach they believe could be used to prepare orthogonal probes for the simultaneous monitoring of several different kinases.

Wang, Q. & Lawrence, D.S. *J. Am. Chem. Soc.* **127**, 7684–7685 (2005).

PROTEIN BIOCHEMISTRY

Dissociation of ligand-receptor complexes using magnetic tweezers

Danilowicz *et al.* describe an inventive way to measure dissociation constants for ligand-receptor pairs. Receptors immobilized onto superparamagnetic beads are allowed to bind to their counterpart ligands, which have been adsorbed to a flat surface. Measurement of the force needed to magnetically separate the pairs permits accurate determination of dissociation kinetics.

Danilowicz, C. *et al. Anal. Chem.* **77**, 3023–3028 (2005).

PROTEOMICS

Global topology analysis of the *Escherichia coli* inner membrane proteome

Membrane proteins comprise a large percentage of the proteome but remain notoriously difficult to characterize. Daley *et al.* used two specialized reporter proteins to reveal the localization of the C termini for over 600 *E. coli* inner membrane proteins; with further computational analysis, this data allowed them to confidently determine the topology for each of these proteins.

Daley, D.O. *et al. Science* **308**, 1321–1323 (2005).

GENOMICS

Clustering and conservation patterns of human microRNAs

Altuvia *et al*. performed a detailed clustering analysis of more than 200 known human microRNAs, and found that miRNA genes tend to have significantly greater clustering than would be expected at random. Via sequence analysis, the group was then able to identify and confirm the existence of 18 additional, new human miRNA genes within or near these clusters.

Altuvia, Y. *et al. Nucleic Acids Res.* **33**, 2697–2706 (2005).

RNA INTERFERENCE

Antibody-mediated *in vivo* delivery of small interfering RNAs via cell-surface receptors

A primary obstacle to the therapeutic application of RNAi is in actually getting small inhibitory RNAs (siRNAs) into target cells. Song *et al.* show that by conjugating siRNAs to protamine-fused antibody Fab fragments, one can achieve efficient targeted gene inhibition in HIV-infected or cancer cells.

Song, E. *et al*. *Nat. Biotechnol.*; published online 22 May 2005.