

progress was made, but we were learning about the uniqueness of the space environment and the difficulties of conducting experiments in a low gravity laboratory. To the uninitiated, some of these experiments may appear "rinky dink" because they are so simple on Earth. However, to complete even a seemingly simple experiment successfully in space is another story.

I heartily agree with the cautionary comments regarding the establishment of institutes. As Lawler indicates, ambiguity of purpose and procedure are serious threats to the success of this reorganization. It is especially difficult to see how handing peer review over to institutes would improve the science.

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References and Notes

1. National Academy of Sciences Space Studies Board, letter to J. Vernikos, 26 July 1995 (<http://www.nas.edu/ssb/csbmvern.html>).
2. See special issues of *FASEB* 4, 1 (1990) and *J. Appl. Physiol.* (suppl.) 73, 2 (1992).
3. The web address of the American Society for Gravi-

tational and Space Biology is (<http://baby.indstate.edu:80/asgsb>).

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Beyond Test Score Comparisons

The Policy Forum, "Myths about test score comparisons" (Dec. 1, p. 1446), by Iris C. Rotberg is on target in emphasizing the damage that can occur in instruction and learning (at primary and secondary schools) if inappropriate practices of assessing student learning are used by those responsible for developing and administering school policy. She presents a degree of caution that needs to be transmitted to state education policy makers who have, without enough caution and questioning, jumped on the so called "authentic assessment" bandwagon.

This caution and concern, however, should not be construed to mean that student assessment and procedures adopted for higher stakes testing by state departments of education cannot be improved. It does not mean that we should eliminate efforts by the National Assessment of Educational Progress (1) to determine the extent to which we are achieving the educational

goals set by the U.S. Congress in 1994 (2).

Reform in the "assessment of student learning movement" is especially significant in the Sciences and Mathematics for several reasons. (i) National education goal number 5 (2, p. 16) specifically addresses these two related subjects. (ii) The *National Science Education Standards* (3) and the parallel document, *Curriculum and Evaluation Standards for School Mathematics* (4) both propose substantial change in teaching and assessment. In a nut shell, both "standards documents" emphasize reducing didactic lecture-verification and increasing inquiry-based instruction through hands-on experiences.

Research and personal professional experiences indicate that the approach teachers use in instruction is often determined by the approach mandated for assessing student learning. Therefore, the desired reform in instructional approach will only occur if reform occurs in assessment. The present system of assessing learning continues to emphasize recall of content, with little emphasis placed on students' abilities to apply higher order thinking (2, 5).

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1. National Assessment of Educational Progress, Educational Testing Service, Princeton, NJ 08541, USA.
2. *The National Education Goals Report Executive Summary* (National Educational Goals Panel, Washington, DC, 1995).
3. National Research Council, *National Science Education Standards* (National Academy of Sciences, Washington, DC, 1996).
4. *Curriculum and Evaluation Standards for School Mathematics* (National Council of Teachers of Mathematics, Reston, VA, 1989).
5. *Performance Assessment: Different Needs, Difficult Answers* (Educational Testing Service, Princeton, NJ, 1995); Office of Technology Assessment, U.S. Congress, *Testing in American Schools: Asking the Right Questions?* (Government Printing Office, Washington, DC, 1992); Project 2061, *Benchmarks for Science Literacy* (American Association for the Advancement of Science, Washington, DC, 1993).

Antisense Research

As a participant in the *Nature Medicine* conference “The Art of Antisense” (held on 21 and 22 September 1995 in New Orleans, Louisiana), I was disappointed by the Research News article, “Antisense has growing pains” (27 Oct., p. 575) by Trisha Gura. The meeting was intended to be a

forum for discussion of the successes and the challenges in antisense research. Gura emphasized some of the early difficulties and negative results discussed in some of the talks and discussions, yet did not include many of the positive results presented at the conference.

There have been several papers demonstrating specific inhibition of gene expression and corresponding biological activity by oligonucleotides in vitro and in vivo using multiple criteria (1). These publications strongly support the idea that oligonucleotides can, in fact, work by an antisense mechanism of action.

Another focus of the conference was the tremendous advances which have been made in the medicinal chemistry of oligonucleotides. Second and third generation oligonucleotide analogs were described which exhibit greater potency, enhanced nuclease stability, altered pharmacokinetic parameters, and potentially decreased toxicity.

What Gura did emphasize was that the proper use of antisense oligonucleotides is a highly demanding and rigorous scientific challenge, as are most scientific endeavors. This view is in contrast to some of the initial approaches taken, when it was thought that simply designing a single oligonucleotide to hybridize to a target gene,

ordering the oligonucleotide from the DNA synthesis lab, and adding it to cells or animals would result in the selective inhibition of expression of the targeted gene product. Today, we know that carefully controlled studies with multiple oligonucleotides, both control and antisense compounds, are required to demonstrate that they are producing a biological effect as a result of the antisense mechanism of action. Identification of active antisense oligonucleotides requires screening multiple oligonucleotides designed to hybridize to different regions on the target mRNA to identify optimal target sites on the mRNA. Furthermore, it was strongly recommended that the initial screens should directly examine the expression of the targeted gene product, rather than test oligonucleotides by an indirect biological process such as cell proliferation.

It has been demonstrated that oligonucleotides, like any other pharmacological agent, exhibit both expected pharmacological activity and unanticipated activity. To expect otherwise would be naïve. However, because an oligonucleotide produces an unexpected effect, such as polyclonal activation of B lymphocytes or binding to extracellular matrix proteins, it does not mean that all observed biological activities are the result of nonantisense effects of the oligonucleotide. Similarly, it is unlikely that all biological effects of antisense oligonucleotides can be ascribed to an antisense mechanism of action. As with any other pharmacological agent, it is important to perform careful dose response curves as well as structure activity relationships, to correlate *in vitro* effects with *in vivo* effects, and to use caution when interpreting data obtained with such agents.

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BIOETHICS Patent News

On the Horizon . . .

CHUGEN BIOSCIENCES (Berkeley, CA) has applied for a covering therapeutic methods utilizing arylate-patient-

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BIOETHICS Patent News

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CENTRE NATIONAL DE LA RECHERCHE Scientifique (France) has patented the use of antibodies which the phenomenon of **ELISA** as selection agents for cells which have been

small grain crops under field conditions and a method for field application of the bacteria to protect soybean crops in small grain crops in a commercial setting. (US

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BIOETHICS Patent News™

Vol. 5, No. 11

Cantor Infringes XOMA sapsis patent

XOMA CORPORATION (Berkeley, CA), of 644-111-1292 (9:00 a.m. - 5:00 p.m.) won its patent infringement suit against **Cantor**, Inc., (Albany, N.Y.), for **1984-1985** revenue - \$70 million when the United States District Court jury returned its verdict against the agency of XOMA patent and finding infringement of it by Cantor. The patent covers the use of certain site-endonome monoclonal antibodies in the treatment of human with gram-negative

XOMA was filed suit against Cantor for infringement of United States Patent No. 4,918,183, which was issued to the **Laboratory of Cantor** in April 1990. XOMA is the exclusive licensee of this patent. In addition to violating the agency of XOMA patent and XOMA's claim of infringement by Cantor, the jury also denied Cantor's claim of implied license to the patent.

The jury trial, which was presided over by Judge Robert H. Schnacke and conducted in the United States District Court for the Northern District of California in San Francisco, began on 10/10/90.

"We are very gratified by the jury's decision," said Steven C. Wendell, chairman and chief executive officer of XOMA Corporation. "We were confident that once the jury members studied the evidence, they would find in our favor."

XOMA initiated the litigation in April 1990, in order to enforce its rights under the '183 Patent. XOMA claimed that Cantor's use of a covering anti-endonome site-endonome therapy, it used in a manner that infringes on the '183 Patent.

In proceedings, Judge Schnacke was content whether to grant further infringement of the '183 Patent.

In support of its claim of infringement, XOMA's testimony pointed to the work of Lowell Young, M.D., who performed research on ES while a professor of medicine at UCLA (Los Angeles, CA). In 1982, Dr. Young published the first scientific paper to describe protection against the lethal effects of endotoxin in a mouse model. In 1984, he co-authored an abstract demonstrating the effectiveness of ES in mice. The first four human patients were treated with ES between February and April of 1988.

XOMA was represented at the trial by the law firm Kaye, Scholer, Fierman, Hays and Handler. Gerald Sork, a senior partner in the firm, was lead counsel.

What is undergoing review by the Food and Drug Administration, constitutes a new treatment for gram-negative sepsis, a massive bacterial infection that kills an estimated 70,000 people in the United States each year. Gram-negative bacteria release into the body a poison known as endotoxin, which is and is itself can result in multiple organ dysfunction. Although antibiotic therapy is highly effective in destroying the bacteria, such treatment is unable to prevent the bacteria from releasing endotoxin. The advantage of ES is that it is designed to bind to and neutralize endotoxin.

Last October, United States Patent No. 5,057,658 issued to Cantor. The patent relates to anti-endonome monoclonal antibodies and their uses.

XOMA is also involved in several class action lawsuits in the same District Court concerning allegations that the company violated federal securities laws and related state laws. These violations involve, among other things, the company's failure to disclose information related to FDA review of the company's application for approval of its ES product for the treatment of gram-negative sepsis.

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