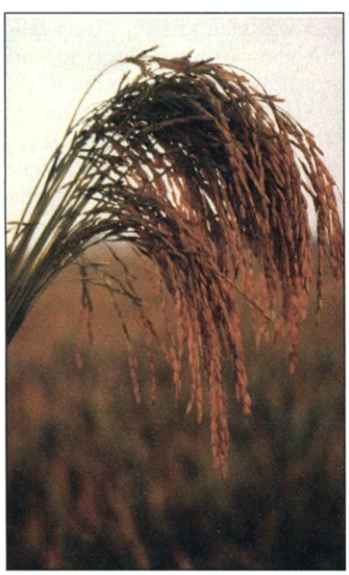
Why Finishing the Rice Genome Matters

A MAJOR PUBLICLY FUNDED GENOME sequencing effort is quietly nearing a milestone. The International Rice Genome Sequencing Project (IRGSP) (http://rgp.dna.affrc.go.jp/rgp/press_releas20011225.htm) has an announced goal of completing a 10-fold redundant draft of a japonica strain of rice by the end of 2002. The primary goal of this ambitious international sequencing effort, the first of a major food crop, is to produce a finished-quality product. The value of draft sequencing to exploit coarse regional syntenic relationships and find genes in a map-based sequence has been established; nevertheless, we do not yet understand how to value a finished sequence or under what conditions its high cost is warranted.



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There are compelling reasons for achieving a publicly available finished rice genome sequence. Rice, at a compact 430 Mb, is only one-sixth the size of the human and maize genomes and provides the sequencing template for all the grasses. This includes every significant grain crop (including sorghum, maize, barley, oat, and wheat), most of which have enormous genomes that are not feasible to sequence at current costs (e.g., wheat has a tetraploid genome estimated at 16 Gb, about five times the size of the human genome). Complete discovery of all rice genes and alignment with the robust genetic map will not only allow immediate fine-grain syntenic leveraging across all the grain genomes but will also provide a critical foundation for all comparative work in agricultural species. Moreover, rice, as a model species, is the plant in which the function of most cereal genes will be discovered.

Not finishing the rice genome will put a surcharge on every grains-related research project in the future. This will be especially true as researchers attempt to understand and harness genes responsible for traits such as disease/drought/salinity tolerance, faster germination time, or nutritional quality in crops such as corn, wheat, barley, rye, oat, sorghum, sugarcane, and millet, as well as rice.

Population growth, loss of arable land, and climatic changes will increasingly challenge the need for continued growth in food supplies. We will need a "Green Gene" revolution to meet this challenge, and completing the rice genome promptly will be the most important step we can now take. We challenge the countries and corporations involved with rice sequencing to find creative and cooperative ways to help the IRGSP complete a finished rice genome by the end of 2003. The potential approach of merging public and private data could form an enhanced draft of the rice genome, similar to Celera's handling of the human genome. Conventional finishing of the IRGSP's bacterial artificial clones (BAC), the Gold Standard option, would be a more easily achieved result. [In fact, one collaboration is already producing results. The Monsanto BACs, which underlie 30% of the BAC/PAC (P1 artificial clone) sequences submitted, have greatly speeded submission of rice sequence to public databases.]

Finishing the rice genome sequence is clearly an opportunity to do something now to benefit all humankind.

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Collaborating on the Rice Genome

MANY INDEPENDENT EFFORTS HAVE NOW been made to sequence portions of or all of the rice genome. The finished rice genome will be instrumental in cereal crop improvement and will serve as a foundation for other cereal genomes. With so much rice sequence now generated, it's time to consider merging these efforts toward a common goal of a finished and accurate genome sequence. Syngenta is making its rice draft sequence available to support the international project (IRGSP). We encourage all genome sequencing groups to join together in establishing a collaborative effort to complete a finished rice genome sequence in the most efficient and timely fashion.

All parties involved in rice genome sequencing are invited to participate. I recommend that participating parties provide sequence assemblies and raw chromatogram data to facilitate finishing of the rice genome and establish an assembly and finishing strategy that maximizes the use of existing data and the current sequencing efforts. In addition, assemblies, quality files, and chromatograms should be made available to all participating parties upon completion. Participating parties should not

Letters to the Editor

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have preferential early access to the entire assembly, and they should collaborate on a finished sequence publication.

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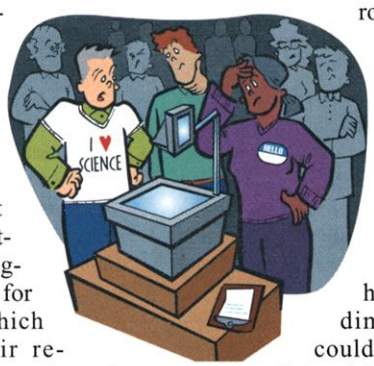
Bowties and Brainiacs at the AAAS Meeting

WHEN I TOLD MY SISTER I'D BE COMING TO Boston for the annual American Association for the Advancement of Science (AAAS) meeting in February, her response was predictable. "These people have their convention on Valentine's Day? What, are they all single? Don't they have lives?"

My response: "I just told you they were scientists."

Billed as the scene "where all of science meets," it was held over 5 days at a sprawling convention center–hotel complex now filled with an avalanche of intellect (if by avalanche we mean predominantly white and gray). There were various lively symposiums such as "The new biology of rocks," "Mathematics and science of origami," and "Rethinking the role of affiliation and aggression in primate groups." "Humans may not be as aggressive and competitive as thought," the Washington University press release for this last session noted, which made me wonder if their researchers had observed and experienced the cunning attacks, jealous rages, and biting of backs commonly associated with top primates engaged in academic peer review.



I next checked out a well-attended seminar on nanotechnology but was disappointed that it didn't really involve any big ideas. I suppose I could have rushed through a lot more sessions like "Animal parts for humans? Xenotransplantation science, ethics, policy and publics," but I didn't want to make a pig of myself. I did make it to a session on Science in Cuba, which started half an hour late, or, as they'd say in Havana, two hours early, compañiero.

The first press briefing I attended was titled "Avian cognition: When being called 'bird brain' is a compliment." Alan Kamil of the University of Nebraska told us how the Clarke's nutcracker can store 25,000 pine seeds every fall and later use spatial memory and landmarks to recover them. He found that one of his graduate students could only recall multiple hiding places with 50% of the accuracy of a Clarke's nutcracker. Of course, the nutcrackers are more highly motivated than grad students, since they can actually live on birdseed.

On Friday morning the President's science adviser, John Marburger, gave a well-attended speech. During follow-up questioning, he agreed that the bulk of the scientific community has reached consensus on human-enhanced global warming. "Everyone understands we have to go to a zero world carbon economy," he explained. Expected White House response, "The President totally agrees with Dr. Marburger that in order to achieve energy independence we have to drill for oil in the Arctic National Wildlife Refuge."

Climate-related panels warned of increased droughts and floods, more rapid sea-level rise, faster glacial melting, and a boom in shark populations around Alaska (which could create competitive pressure on members of the State Bar). The good news? Urban smog and pollution may be slowing the rate of heating by contributing to reflective cloud formation. Between that and the bioterrorism ballroom event, I was glad to see NASA sponsoring an alternative panel, "Interstellar travel and multi-generation space ships."

Later I attended a session where French physicist Maria Spiropulu explained her theory of the fourth dimension and how one couldn't literally be sucked into a black hole, which still left the unanswered question, so where did all those Enron billions go?

Unfortunately, one great technological challenge continues to stymie America's top scientists. I was deeply moved by how many continue to struggle with overhead projectors that often delay, distort, or simply make a mockery of their carefully arranged transparencies. Although it's admittedly easy to ridicule science and its culture (and fun too), I still have to acknowledge a modest sense of awe as I learned about cutting-edge discoveries in human origins (monkeys you say?), astronomy, behavioral genetics, and brain structure (I think, therefore my prefrontal cortex neural mechanisms are functioning).

I certainly experienced a sense of wonder staring at a picture of a transistor the width of a single electron. I wondered what kind of batteries it came with.

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Regulating Natural Health Products

IN HIS RECENT EDITORIAL "THE FUTURE OF medicine" (11 Jan., p. 233), C. Everett Koop calls attention to the growing use of alternative medicine and the need to prove the efficacy and safety of dietary supplements. He is correct when he compares the current situation to the snake oil days of a century ago that led to passage of the Pure Food and Drug Act of 1906. However, in 1994, Congress passed the Dietary Supplement Health and Education Act (DSHEA), in response to a massive lobbying effort by the natural products industry. This law exempts the manufacturers of dietary supplements from having to prove safety or efficacy before marketing. The burden of proof is thus on the Food and Drug Administration (FDA) to show that something is not safe, and to do this, the FDA must rely on an inefficient system of voluntary reporting of adverse events. The net result of this is a relatively unregulated industry that was estimated to have sales of $17.1 billion in 2000 (*1*).

Koop calls upon the "natural products industry to work with medical research, including the FDA" to assure safety and efficacy. While this is certainly something that should happen, it is naïve to think that it will occur in the absence of regulatory requirements. Although many in the industry support the FDA's proposed Good Manufacturing Practices (which address only issues of quality control), the industry has no incentive to voluntarily fund research that might reveal that some products are neither safe nor effective.

Congress must repeal or amend the DSHEA to give the FDA the power to regulate nutritional supplements by requiring scientific proof of efficacy and safety. Until that happens, it is essential that adequate resources be made available to the FDA and the Federal Trade Commission to enforce existing rules covering claims made on labels and in other advertising. Manufacturers should also be required to label all dietary supplements with a toll-free number and a Web URL for reporting adverse events directly to the FDA (*2*).

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References and Notes

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2. J. C. Lashof, Testimony before the Senate Select Committee on Aging, 10 September 2001.

CREDIT: TIM SMITH