Ownership and human genome

SIR — A recent leading article (*Nature* **371**, 363–364; 1994) addresses ownership of the human genome and weighs private commerce against the public good. The editor acknowledges the apparently unselfish way in which the academic community has published sequence information in public databases, but questions why a profit-making company would publish its sequence data in the same public forum. Certainly it is not merely a question of commercial versus academic motives. The issue is complex and involves an underlying philosophy regarding basic research. After in-depth analysis of this situation, Merck has taken the policy position that certain information relating to the human genome should not be the subject of exclusive ownership. Why should we take this position?

The sequences of expressed genes have been determined with increasing speed and ease. The main commercial use of sequence information has been for construction of protein expression systems for use in drug screening. In this light, Merck has worked to discover and utilize expressed genes as targets for drug discovery. The results of such work has been protected through the patent processes when warranted, and broadly published in both the literature and electronic databases. Physical resources used in this work have generally been made available to both commercial and academic researchers on a non-exclusive basis. This approach, shared by many others, has proved successful for Merck, and has not detracted from our commercial advances.

The set of expressed human gene sequences that is being defined by the EST (expressed sequence tag) approach, pioneered by Matsubara, Sikela and Venter, represents an important and evolving resource for genome research, and provides a potential basis for future biomedical research. EST sequencing may lead to nearly complete gene identification far in advance of the complete sequencing of the human genome. It is this prospect that is most exciting to both commercial and academic concerns. We agree with the editor that "better medicines must come from the identification of genes whose products are involved in metabolic disturbances linked with disease". Yet no current methodology exists that can reliably capitalize on gene sequence information for drug discovery, except for the rare direct use of the expressed protein as a therapeutic. The route from discovered gene to developed drug is long, expensive and has a high failure rate. Biological understanding of the gene and its products in both physiology and pathophysiology is necessary for the validation of a given gene as a potential drug target. In a few selected cases, the gene or its protein product may have direct therapeutic utility, but for the vast majority of expressed genes the principal value will be as a research tool, one of many, in the drug development process.

Patent protection should encourage the advancement of technology and the creation of saleable products. A key question centres on the determination of the value of intellectual property whether it may or may not be subject to patent protection. Clearly, in the matter of ESTs, the patentability issue remains uncertain, leading several key commercial sequencing concerns to keep their sequences as trade secrets. This fact alone is not uncommon, nor unexpected. However, it is the use of these secret sequences to secure closed collaborations on their biological investigation, and to secure commercial rights to the biological discoveries that result, that created consternation in the academic and commercial research communities.

Against this background Merck has taken the initiative to create a public database of expressed human genes. By providing the necessary resources to some of the most advanced and experienced laboratories, a large-scale, coordinated public EST sequencing effort can be developed. The total set of human genes contains critical information for the understanding of human biology, but we need to develop new methods to extract that knowledge. The complexity of this process will require the intellectual and experimental resources of the world's best biologists for ultimate success. The resulting discoveries should clarify the true commercial potential of these genes.

Since scientists at any research institution, including Merck, can say that "most research occurs elsewhere", we believe that providing broad access to human gene sequences optimizes the possibility that the information will be used to benefit human health. As this extended process creates intellectual property, patent protection can and should be sought by the inventors, and appropriate commercial activities such as drug development will be encouraged. In summary, we believe that the Merck initiative will accelerate the gene discovery process, and that in turn the development of novel therapeutics to benefit human health will also be accelerated. Over the years Merck has sought to make basic research tools broadly available and to work closely with academic scientists, and this will remain our strategy for the future.

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Drug testing

SIR — A recent leading article in *Nature* (**371**, 90; 1994) comments on drug testing of athletes. It points out that positive results from tests on well-known athletes are invariably made public, and asks why negative results are not also made public so that the prevalence of drug-taking by athletes can be assessed. A drug-testing policy should properly explain how confidentiality of test data will be protected in the event of a confirmed positive test result; and access to testing data, whether the results are positive or negative, is a potentially litigious area[1].

It would be in any case difficult to ascertain the true incidence of drug use by athletes, because many athletes know when to take drugs, at what dose level, and when to stop in order to test negative at competitions[2]. Indeed, some feel that drug testing of athletes can be effective only if carried out on a random, unannounced basis throughout the year[3–4]. Random testing, however, may raise legal problems. Moreover, most abuse of supposed performance-enhancing drugs may occur in local sports clubs rather than in the competitive arena.

Even in the best of circumstances, the practice and theory of drug testing suffers from potential flaws and limitations[1]. Available testing technology for urine samples has distinct limitations; and it is thus quite important to consider the 'sensitivity' of particular screening procedures as well as the 'specificity' of extant confirming procedures. Positive test results should be confirmed by a different test. Your leading article asks why, if there are always two urine samples, they are not analysed independently at separate laboratories. Confirmation of a positive result by a different test in a different laboratory, or the independent analysis of two samples at separate laboratories, would add protection.

Further rigorous study is needed of the technical issues raised by drug-testing programmes for athletes, covering selection of athletes for testing, the timing of drug testing, consent forms, preparing a list of banned susbstances, and procedures for the handling, collecting and transporting of drug-testing samples[1]. The emphasis, however, should be on educating and motivating athletes not to abuse drugs, rather than simply conducting drug testing and then 'punishing' those testing positive for proscribed substances.

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