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deCODE deferred

To the editor:

It may be of interest to your readers to learn that the Icelandic government has now been forced to postpone a bill designed to give deCODE Genetics an exclusive license to collect current and retrospective medical information about all Icelanders into a centralized, comprehensive database (see *Nature Biotechnology* 16:225–226, March 1998 and 16:337–340, April 1998). The company would then have the sole right to commercial exploitation.

The bill took the Icelandic medical and scientific establishment completely by surprise. The existence of the bill was unknown to everyone here except the government and leading executives of deCODE until its announcement on March 31. No discussion had thus taken place on the desirability or otherwise of the measures in the proposed bill. It became clear that the government intended to rush the bill through parliament to forestall debate. Following very strong opposition from the medical and scientific community, the bill was postponed to the autumn.

There are three major concerns. First, is the database justifiable on scientific, economic, and ethical grounds. Second, should the database be a commercial asset of a private company. And, third, is it right to offer a single company legalized monopoly control. If the bill became law, it could be used to restrict the research of Icelandic scientists who work in the medical field and wish to remain independent of deCODE Genetics.

Another cause for concern in the scientific community is the Icelandic tissue bank which holds samples that go back some 40 to 50 years. The access to samples from the bank will be governed by a new law. The contents have not yet been disclosed.

There are advantages to studying genetics in the Icelandic population. What has not been shown is that the commercial exploitation of a nationwide database and tissue bank would further genetic research. Many questions of ethics and confidentiality remain unanswered in the proposed legislation. It is to be hoped that the oldest parliament in Europe does not let democracy slip in order to allow one company the right to order legislation exclusively for its own ends.

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Unfair treatment

To the editor:

After reading Vicki Brower's "Prostate cancer link sours IGF-1" (*Nature Biotechnology* 16:223, March 1998), I felt compelled to reply to this rather one-sided analysis of IGF-1 therapy. While talk continues of the "side effects" of IGF-1, few of these side effects, other than retinal changes, edema, facial nerve palsy, dyspnea, and tachycardia, have led to long-term sequelae. They have simply required stopping the drug in these individuals. As we are all aware, there are no drugs that have no side effects; thus, discontinuation of a drug in some individuals who suffer side effects does not warrant a "death sentence" of that drug.

Brower highlights the one study suggesting that serum IGF-1 levels correlate with the risk for prostate cancer. This is a population-based study that is incapable of showing any cause-and-effect relationship between IGF-1 and cancer, a problem commonly found with such studies. Thus, this study in no way reflects the pharmacologic use of IGF-1. For instance, IGF-1 has been used in patients with growth hormone insensitivity who have low levels of circulating IGF-1. IGF-1 has been shown to restore these children to a more normal growth pattern. Likewise, patients with type 1 diabetes have low levels of IGF-1 and a disordered production of the various serum carriers of IGFs, the IGF-binding proteins. In several studies, researchers have shown that subcutaneous administration of IGF-1 to type 1 diabetics restores serum total and free IGF-1 levels to a normal range and restores most of the IGFBPs to their normal concentrations. Furthermore, patients in these studies benefited from marked improvement in glycemic control, not "marginal benefits," as suggested by Ms. Brower. Thus, it appears that IGF-1, when used in IGF-1-deficient populations, has beneficial effects.

Although the long-term side effects of IGF-1 therapy may not be evident now, this type of analysis is like comparing apples and oranges. Unfortunately, due to such hard-line viewpoints as expressed in the article, IGF-1 is now unavailable to investigators and their patients with IGF-1 deficiencies.

Without further studies in such promising areas, patients—especially children with growth hormone resistance and type 1 diabetes—will not have access to what appeared by all accounts to be a very successful intervention.

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Gene therapy or antisense

To the editor:

With statements by Friedman[1] that gene therapy, while not a failure, is simply too immature to deliver on its promises, and Varmus[2] that gene therapy is not ready for prime time, earlier excitement about the field has cooled, despite some successes[3]. And as the US National Institutes of Health has spent $200 million on gene therapy, and the private sector much more, it appears that every route to success has been explored, but a clear path not yet found. Zamecnik proposed the use of synthetic antisense oligonucleotides to selectively and specifically block target gene expression at about the same time that gene therapy was first promoted. His proposal was largely ignored until the beginning of the 1990s.

Simple approaches are often overlooked in science, yet are often the ones that work. The prevalent feeling in the antisense field was that antisense oligonucleotide therapy would work only in vitro, inhibiting gene expression for short periods, thus limiting its use. However, the most recent literature disproves this feeling, opening a new era for antisense technology. In vivo trials have been successful, and it has been realized that antisense may not only inhibit gene expression but also correct a wrong splicing of pre-mRNA.

The future for therapeutic antisense is very bright: By using stabilized analogs and carefully using encapsulating liposomes, many groups now obtain a specific effect in vitro using concentrations below 1 μM; this is promising for in vivo use. Specificity can be improved by manipulating the fatty acid composition of phospholipids used to prepare liposomes, as well as new technologies such as osmotic pumps. Once we have understood more about mechanism of action of antisense drugs, they are likely to surpass gene therapy in the run to the pharmacology of the third millennium.

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1. Friedman, T. 1996. *Nature Medicine* 2:144–147.
2. Touchette, N. 1996. *Nature Medicine* 2:7–8.
3. Bordignon, C. et al. 1995. *Science* 270:470–475.