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Please send letters to:
Nature Biotechnology
345 Park Avenue South
New York, NY 10010-1707, USA
Fax: +1 212 696 9635
E-mail: m.francisco@natureny.com

Single nucleotide polymorphism wars?

To the editor:

Your editorial, "Moving genomics from discovery to development" (*Nature Biotechnology* 15:923, October 1997) illustrates how pharmacogenomics, the recent avatar of pharmacogenetics—a decades-old vision of tailoring drugs to a patient's genetic makeup—is catching the limelight of the drug discovery scene, triggered by the growing amounts of data output, directly and indirectly, by the Human Genome Project. While for some, drug discovery has now entered a "postgenomic" era (*Nature Biotechnology* 15:1220, November 1997), and for others "functional genomics" is the order of the day (*Science* 278:601–602, October 1997), there is much more at stake than meets the eye.

The feeling of urgency surrounding the promotion of the US National Institutes of Health (NIH)–backed project of collecting single-base variations in human DNA (*Science* 278:1580–1581, November 1997) into publicly available databases, may be heralding a war between industry and academia. Because the latter single nucleotide polymorphism (SNP) databases can be put to immediate use to accelerate the development of efficient tests to help stratify populations for trial design, they are of tremendous economical interest.

Worries over the patentable character of SNPs, and particularly of those found in protein-coding regions (cSNPs), have surfaced in academic circles. The recent joint venture between the Chicago-based drug manufacturer Abbot Laboratories and the Paris-based Genset (*Nature Biotechnology* 15:829, 1997), or the collaboration between Santa Clara-based biochip maker Affymetrix and geneticist Eric Lander's lab at the Massachusetts Institute of Technology, have exacerbated the feeling among academics that private companies might snap up SNPs, and specifically the less numerous cSNPs, and patent them, reaping the financial benefits and keeping smaller labs at bay.

Indeed, venture capital-backed companies such as Variagenics (Cambridge, MA) or Genaissance Therapeutics (New Haven, CT) are budding today. Their survival, however, depends on securing further private investment and thus on continuing to patent human genetic variation. The whole argument is reminiscent of the heat surrounding the Java debate in the software industry, another high-tech industry highly favored by venture capital funds.

In recent litigation, suing and countersuing archrivals computer manufacturer Sun Microsystems and software giant Microsoft started fighting for control of the development of the Java programming language and development platform. Tension has been building up over the past year, fueled by worries from the Java developers' community that Microsoft could single-handedly alter the Java programming language by corrupting its touted "open and portable" nature—the promise of which was precisely what prompted new Java startups to sprout by the hundreds in the past couple of years, heftily funded by private investors.

In a bizarre twist of the usual way standards are edicted, Sun Microsystems recently became the first for-profit company to make it as publicly available specifications (PAS) submitter to the International Standards Organization (ISO), which will enable it to submit Java to become an ISO standard (*Unigram.X* 667:5, November 1997).

Whereas it is the data, in the case of drug discovery, or the technology, in the case of Java for the software sector, it is, in both occurrences, the essence of the platform on which further developments will be blossoming that is at stake. The short-term decisions that are imminent will shape their respective industries for the foreseeable future. The new generation of private investors in information and in life sciences technologies—often in both in the same fund management company—is certainly literate enough to arbitrage between the short-term issues with the unavoidable amount of hype and me-too-ism that surround them, and the longer term solutions where the higher returns on investment are found.

Jean-Marie Chauvet
Dassault Development
9, rond-point des Champs Elysées
75008 Paris, France
(jchauvet@worldnet.fr)

Xenotransplantation moratorium

To the editor:

We note in your report, "Xenotransplant firms get xenophobic" (*Nature Biotechnology* 15:1239, November 1997) the suggestion that the conclusion in the Kennedy Report[1] of the United Kingdom Advisory Group on the Ethics of Xenotransplantation (UK AGEX) for "a temporary moratorium on xenotransplantation. . ." was driven by ". . .events unconnected with xenotransplantation itself. . .," namely the bovine spongiform encephalopathy (BSE) and new variant Creutzfeldt-Jakob disease (nvCJD) debate. As chairman [Prof. Kennedy] and member of the erstwhile UK AGEX we would like it placed on record that our conclusions were in no way based on, or driven by, the BSE/nvCJD discussions. Rather, they were based on the committee's analyses of the published studies of xenotransplantation and broad consultations and deliberations in and outwith the committee. We concluded that at the time of the writing and indeed the publication of our report there was inadequate knowledge to justify a move to clinical xenotransplantation. Our concerns related primarily to three areas: risk of infections, problems associated with immunological rejection, and efficacy/functioning of transplanted organs.

Regarding risk of infections, we concluded that there was insufficient knowledge about the known viruses to make it safe to proceed to clinical trials at the current time and we stated that that was particularly relevant to the porcine endogenous retroviruses[1]. Indeed, since the publication of our report this conclusion has been further justified by additional peer-reviewed published reports pertaining to the potential risk of porcine retroviruses[2,3].

Second, regarding graft rejection, we considered that the evidence on immunological rejection (particularly that beyond hyperacute rejection) was too limited to justify a move to clinical trials. We recommended that further research should be carried out to investigate more fully the rejection processes associated with xenotransplantation and to determine an effective and acceptable immunosuppression regimen. Again, peer-reviewed science published after our report has amply justified the need for greater awareness and study of the problems associated with these additional forms of immunological rejection[4,5].

Third, regarding organ function, we concluded that the evidence on transplant function, organ growth, and the functioning of the recipients' immune system within the transplant was too limited to justify a move to clinical trials.

In summary, our conclusions were based on the best available objective scientific evidence. Indeed, following our report it is noteworthy that many of the leading scientists and clinicians in the field of transplantation in academia[6] were supportive of our conclusions.

Ian Kennedy
Erstwhile Chairman UK AGEX
School of Public Policy
University College London

Herb Sewell
Erstwhile Member UK AGEX
School of Clinical Laboratories Sciences
University of Nottingham
(Herb.Sewell@nottingham.ac.uk)

1. The Advisory Group on the Ethics of Xenotransplantation, Animal Tissue into Humans. London: Department of Health 1997.
2. Le Tissier, P. et al. 1997. *Nature* **389**:681–682.
3. Stoye, J.P. 1997. *Nature* **386**:126–127.
4. Bach, F.H. et al. 1997. *Nature Medicine* **3**:944–948.
5. Kobayashi, T. et al. 1997. *Transplantation* **64**:1255–1261.
6. Morris, P.J. 1997. *Brit. Med. J.* **314**:242.