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Digital DNA signatures for animal tagging

To the editor:

Verification of identity and parentage of animals is essential for the efficient management of animal populations and for assessing animal food safety. Recently, DNA-based tests, specifically the analysis of microsatellites, have been introduced for identity verification and parentage control of livestock. In this context, we propose that a standardized set of single nucleotide polymorphisms (SNPs) be adopted as an alternative to microsatellite analyses. To facilitate this approach, we have established a database (http://www.SNPZoo.de) that can serve as a depository of SNP information in livestock species.

The main advantages of SNPs are the low mutation rate, the suitability for standardization, and that they do not require a specific typing platform. Standardization consists of the selection of appropriate SNP loci and establishment of the order in which the genotypes are presented. For a given species, each SNP of this standardized set is unambiguously identified by its unique flanking nucleotide sequence. Each SNP position is queried for the presence or absence of a specific base, resulting in a string of binary answers (10, homozygous allele number 1; 01, homozygous allele number 2; 11, heterozygous; and 00, assay failure) that we term a digital DNA signature.

We hope that establishment of the database will facilitate the standardization process. It contains information on the SNP loci themselves as well as corresponding allele frequency data in a standardized fashion. It is possible to submit information on new variant sites or population data for previously identified SNPs. The goal is to compile, from a large collection of SNPs, a set of SNPs that would allow exclusion powers of >99.99% for parentage control and probabilities of identity of $<10^{-11}$ for individual identification in each population. Forty SNPs with an average frequency of the minor allele of 20% will yield an exclusion power of 0.99994 and a probability of identity of 2.66073×10^{-12} (ref. 1). There are numerous SNPs with a frequency of the minor allele >20% in several populations and probably even throughout a species, resulting in overlapping sets of SNPs, each set optimal for a different population.

We propose to define 96 SNP positions for the bovine species. Similar standards may also be established for other species. For analyses in a given population, single-nucleotide queries can be restricted to the most polymorphic sites for this population. For each signature, the associated probability of identity and the exclusion probabilities should be indicated to qualify exclusion in parentage control or a signature match in identity control. The first position of the signature will be reserved for the result of a gender query. The standardized format of SNP data will facilitate the maintenance of the allele frequency databases that will be necessary for calculating the exclusion powers and probabilities of identities. Such frequency databases will be an excellent tool for genetic diversity analyses. The proposed standard and the independence from a specific typing platform will be essential to ensure competition on the market for genotyping services and thus low-cost digital DNA signatures. Cost-efficient typing of entire animal populations for the consequent tracing of animals and animal products will become realistic.

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PERV clarification

To the editor:

It was with interest that I read the article on regenerative medicine in the March 2001 issue (*Nat. Biotechnol.* **19**, 201–206, 2001) and was pleased to see the coverage given to xenotransplantation and other technologies as a potential solution to the chronic shortage of human donor organs and tissues.

In reading your article, however, I noted an inaccuracy. It was reported: "Biotransplant has bred miniature swine free from PERV." This statement is incorrect and requires further clarification. To assess the potential for the lineages of BioTransplant miniature swine to transmit replication-competent PERV, peripheral blood and aortic endothelial cells were co-cultured with human and porcine target cells using standard assays. In all cases, transmission and replication in the porcine target cells was detected. However, a single line of miniature swine was identified that failed in all tests to establish infection in human cells. As such, these animals are not free from PERV. Rather, they appear not to produce PERV that can establish a productive replication in human cells. This observation (C. Patience, unpublished data) has also been confirmed in two independent laboratories. Defining the genetic basis of this behavior in this line of miniature swine is now the focus of safety research at Immerge BioTherapeutics, a recent joint venture between Novartis Pharma AG and BioTransplant Inc.

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Errata

On page 105 of the February 2001 issue, the Business and Regulatory News Analysis article entitled "Indian regulatory system stifles industry growth" by K.S. Jayaraman contained a statement concerning the suppression of private-sector drug development by the public sector that was mistakenly attributed to S.K. Kapur, managing director of Pro Agro Seed Company. The statement should have been attributed to Arvind Kapur, managing director of Nunhems Pro Agro.

On page 195 of the March 2001 issue, the commentary entitled "Genomics and human life span—what's left to extend?" by Richard C. Strohman contained mistakes in the reference citations and reference list. Reference numbering in the text was incorrect and references 2 and 4 should not have been present in the list. A corrected form of the article can be found at http://biotech.nature.com/journal/v19/n6/index.html.

On page 410 of the May 2001 issue, the Feature article entitled "Public biotech 2000—the numbers" by Riku Lähteenmäki and Liz Fletcher contains the incorrect statement that Monsanto was acquired by American Home Products last year. Monsanto was actually acquired by Pharmacia & Upjohn last year.