anticipate two potential sources of error; these being if the transgene has inserted into the pseudo-autosomal region (whereby likelihood of recombination between the X and Y chromosomes is increased), or non-disjunction during male meiosis (giving rise to phenotypically male green fluorescent mice of XXY genotype). To date, over 500 offspring have been examined either by PCR or using morphological landmarks, and no deviations from the expected sex outcome have been observed.

We believe the D4/XEGFP transgenic line to be the first reported case where a non-invasive marker has been used for sex selection in any organism before sexual dimorphism makes the discrimination possible. Our results suggest that autofluorescent protein tagging of sex chromosomes should allow non-invasive sexing of progeny, not only in mice, but also in a wide variety of other organisms, thereby creating more efficient and cost

effective breeding regimes for agricultural production.

The D4/XEGFP mice have been maintained on both outbred (ICR) and inbred (129/Sv-cp) backgrounds, and will be available from the Jackson Laboratory Induced Mutant Resource as TgN(GFPX)4Nagy.

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**Anna-Katerina Hadjantonakis¹,
Marina Gertsenstein¹, Masahito Ikawa³,
Masaru Okabe³ & Andras Nagy^{1,2}**

¹Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 600 University Avenue, Toronto, Ontario M5G 1X5, Canada.

²Department of Molecular and Medical Genetics, University of Toronto, Toronto M5S 1A8, Canada. ³Research Institute for Microbial

Diseases, Osaka University, Yamadaoka 3-1, Suita, Osaka 565, Japan.

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Human genome annotation—a possible role for HUGO?

The recent editorial in this journal (*Nature Genet.* **19**, 1–2, 1998), raising critical issues around the future role for the Human Genome Organisation (HUGO), was very timely, and I share many of the reservations that were voiced in the article. In part, HUGO's difficulties have arisen due to an inevitable tension between those who fund research and an organization which sought to influence its development without substantial financial input.

The Human Genome project is now firmly in the sequencing phase. This has initiated a continuing discussion as to how the sequence should be annotated—that is, how the biology intrinsic to the sequence can be documented. In part, this discussion has tended to be focused upon computerized annotation, and it is the task of the bioinformatics community to develop this annotation to its highest levels of accuracy and completeness (see, for, example Wheelan, S.J. & Boguski, M.S. *Genome Res.* **8**, 168–169, 1998). This form of annotation includes computerized analysis of the sequence to identify genes, sequence structures such as promoters and repeats, base-composi-

tion asymmetry and large-scale organization, and provision of very extensive cross reference to external databases including those for the scientific literature and genetic disease.

This is a necessarily narrow interpretation of annotation; in a wider sense, annotation can be the products of any biological observation that relates back to the DNA sequence. Such annotations derive from wide areas of biology. It is likely that they will include the wealth of experimental data relating to gene expression and its differential control, the relationship of DNA sequence to human variation and disease (including gene mutations, gross chromosomal rearrangements and mutability of DNA sequence), the population biology of human DNA variation, the evolution of the genome and its relationship to the genomes of model organisms and, finally, the relationship of DNA sequence to chromosomal architecture.

It is not all that clear that computerized methods alone will be able to develop this type of annotation. I would argue that to properly annotate the human sequence with the consensus clinical, population,

genetic and biological data drawn from the wider scientific community, will require the work of human curators for many years after the sequence has been generated. At present, we do not have any obvious mechanism for facilitating, standardizing or coordinating this. I would like to suggest that an international organization is the obvious vehicle for assuming such a role, particularly because it is the annotation that is likely to contain the most ethically and socially sensitive information about our genes.

The dissociation of annotation and long-term curation from the expensive task of acquisition will also allow a very different interaction between end users, the international coordinating body and the funding agencies. I do not wish to suggest that HUGO as it is currently configured is necessarily the best organization to carry out this task, but I believe that it may well provide the model structure. If HUGO dies, it is likely we will have to reinvent something very similar.

Peter Little

Department of Biochemistry, Imperial College of Science, Technology and Medicine, London SW7 2AZ, UK. e-mail: p.little@ic.ac.uk