ETHICS WATCH

Public perceptions and regulatory policy

There are many reasons why the field of biotechnology is particularly difficult to regulate. It is complex, the relevant science moves forward quickly, and the risks and benefits that are associated with it are not always easy to identify or agree on. However, I believe that the diverse and changing nature of public perceptions stands as the single greatest regulatory challenge in this area.

The international debate over "therapeutic cloning" is a good example of the dilemma. During the past few years, governments throughout the world have been struggling with how best to regulate both reproductive and therapeutic cloning. Although the public clearly endorses a ban on reproductive cloning, the available opinion data on therapeutic cloning paints a more complex picture. Most research on public opinion has found strong support for stem-cell research and, even, a degree of support for the concept of therapeutic cloning[1]. However, for some citizens — about 20% in Canada — no amount of potential social or scientific benefit will justify this type of research. As such, policy makers are left without a clear public mandate. Recently, the US President's Council on Bioethics explicitly noted this lack of consensus, and therefore concluded that a ban on all forms of human cloning was not justified and that a moratorium should be imposed to give time "to seek moral consensus"[2]. (I suspect that this "moral consensus" will remain elusive.)

Public opinion will also change. And, rightly or not, history tells us that this change is likely to be in the direction of increased public support (or, at least, increased ambivalence). *In vitro* fertilization, sperm donation, the transplantation of human organs and research involving cadavers were all activities that were first met with a degree of public resistance.

We should not make laws solely on the basis of opinion polls — a methodology with inherent limitations. However, we must also accept that, for many areas of biotechnology, it will be difficult to justify regulatory policy on broad consensus alone. I believe that the best way to deal with this inevitable state of affairs is to avoid the use of rigid statutory prohibitions and, instead, to establish regulatory bodies with the power to oversee particular areas of biotechnology[3]. The regulatory body should be interdisciplinary, have the necessary expertise and a public engagement and education mandate, and be appropriately accountable. Whereas statutory bans are often difficult to enact or change, a regulatory approach can accommodate emerging science and new social concerns. And because a regulatory body can serve as a forum for continuing public debate, it can remain sensitive to the public's moral ambiguity concerning much of biotechnology.

Timothy Caulfield is at the Health Law Institute at the University of Alberta, Canada.

Timothy Caulfield

REFERENCES

[1]Scoffield, H. Canadians favour limited use of clones for emergencies only, survey finds. *Globe and Mail* A2, 16 June (2000) | [2]The President's Council on Bioethics. *Human Cloning and Human Dignity: An Ethical Inquiry* (Washington, DC, July 2002) [online] <http://www.bioethics.gov/cloningreport/fullreport.html> | [3]Knowles, L. Science policy and the law. Reproductive and therapeutic cloning. *NYU J. Legis. Public Policy* **4**, 13 (2001)

GENE MAPPING

More than just a pretty face

For nearly 20 years, some sheep have flaunted what must be every vain person's dream: a genetic variant that confers beautiful buttocks, commonly known as the callipyge phenotype. More prosaically, the single-locus mutation responsible for the phenotype causes muscle hypertrophy, and it does so through an unusual genetic means, known as polar overdominance. This means that animals only manifest the phenotype if they are heterozygous for the callipygous variant and only if the variant has been inherited from a particular parent (in this case, the father). Freking and colleagues have now pinpointed the single base change in the gene, *CLPG*, that underlies the callipygous trait. Breeders and geneticists alike have a stake in this discovery: leaner meat could be bred as a result, and we could gain a better understanding of the epigenetic mechanisms that underlie the inheritance of the phenotype.

Previous efforts to map *CLPG* had localized it genetically to a small (400-kb) telomeric region on chromosome 18 — small enough to make a direct-sequencing approach to finding the variant a realistic goal. The high level of background polymorphism in sheep, however, made it impossible to detect the causative SNP simply by comparing affected heterozygotes to normal homozygotes. The authors therefore turned to the pedigree of the particular flock they were studying for some help. One callipygous ram in particular was key: the critical region of both copies of chromosome 18 in this ram were probably identical-by-descent, apart from the presence of the *CLPG* mutation on one copy. Comparing the sequence of the ram to a panel of informative genotypes uncovered 616 polymorphisms, but only one of them — an A to G change — could be uniquely assigned to the callipygous trait. The G allele was never found in sheep of diverse breeds, so validating further the pedigree-screening approach as the most robust there is for finding the causative variant of a phenotype.

It's taken ten years, but an important aspect of the callipyge phenotype has now been found, heralding the starting point for understanding what the *CLPG* variant does. The *CLPG* region is conserved in cattle, human and mouse genomes, and the variant might be incorporated into an RNA transcript, but little else is known about its function. Initial attempts to detect whether the variant has some regulatory effect — for example, by altering the imprinting status of the region — have been unsuccessful. Clearly more work is needed to get to the bottom of this trait.

Tanita Casci

References and links

ORIGINAL RESEARCH PAPER Freking, B. A. *et al.* Identification of the single base change causing the callipyge muscle hypertrophy phenotype, the only known example of polar overdominance in mammals. *Genome Res.* **12**, 1496–1506 (2002)