ETHICS WATCH

PGD: new ethical challenges

More than 1,000 children have been born following preimplantation genetic diagnosis (PGD). PGD use is likely to grow over the next decade, mostly as a tool for detecting aneuploidies in *in vitro* fertilized (IVF) embryos but also for screening an increasing number of mutations that are related to health and disease[1]. Some have decried these steps as moves towards creating "designer children", but recent evidence fails to support this view.

First developed as an alternative to amniocentesis for screening embryos for autosomal and sex-linked diseases, PGD is now used to screen for other genetic mutations, for disease susceptibility and to identify prospective children who can make haematopoietic stem cell donations to existing children[1]. Unless one objects to screening embryos (and many do), these new practices should be ethically acceptable to those who otherwise accept PGD.

More controversial is PGD for non-medical uses, such as sex selection, because of the risk that sex selection, particularly of firstborns, will discriminate against females. The ethical assessment shifts, however, when the sexes of only second, or later, children are chosen. If no sex is disproportionately favoured, the threat to women and the risk of unbalanced sex ratios are considerably reduced. Ethical debate then focuses on whether desire for family 'gender balance' justifies IVF and embryo screening[2]. While many will oppose this practice, we are likely to see an increased acceptance of PGD for this use.

Until genes for other phenotypic traits are identified, embryo screening for other non-medical purposes is unlikely to occur. Potential candidates at present include the *GJB2* gene mutations, which are the largest known contributor to inherited deafness[3]. Individuals with a family history of deafness might request PGD to screen for *GJB2* mutations, therefore raising concerns about prejudice to the deaf community. If screening could occur without hurting the rights or interests of deaf people, its use to ensure a hearing child might be accepted. However, what if deaf couples want to screen for embryos with these mutations? In addition to questions about whether embryos should be discarded for such a choice, the ethical issue is whether being deaf, instead of hearing, will hurt a child. Given the rich culture now available to deaf people, many bioethicists would accept the deaf parents' choice[4].

These examples illustrate the ethical issues that will arise from new uses of PGD. More debate is clearly needed, but evidence indicates that, when new uses of PGD help parents to have healthy, wanted children, society is likely to accept them. If so, public authorities should focus on ensuring the techniques' safety, reliability and availability, and not on stopping PGD as the harbinger of "designer" children.

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Yin/Yang, blue purple, by Jaques Deshaies (2002) (detail).

REFERENCES

[1]Braude, P. *et al.* Preimplantation genetic diagnosis. *Nature Rev. Genet.* **3**, 941–953 (2002) | [2]Robertson, J. A. Sex selection for gender variety by preimplantation genetic diagnosis. *Fertil. Steril.* **78**, 463 (2002) | [3]Nance, W. E. & Pandya, A. in *Genetics and Auditory Disorders* (eds Keats, B. J. B., Popper, A. N. & Fay, R. R.) 67–91 (Springer, New York, 2002) | [4]Levy, N. Deafness, culture and choice. *J. Med. Ethics* **28**, 284–285 (2002)

DEVELOPMENTAL BIOLOGY

Regeneration swims into view

One reason why we know relatively little about the biological basis of complex tissue regeneration is that it has been traditionally studied in vertebrate organisms — such as the newt — for which genetic tools are not available. Kenneth Poss and colleagues now suggest a solution to this problem: zebrafish. These fish can regenerate an impressive number of adult structures, from fins to spinal cord. Combine this with their genetic tractability, and you have the ideal vertebrate organism in which to study regeneration, as Poss *et al.* illustrate with their recent findings.

To investigate the genetic basis of fin regeneration, the authors mutagenized zebrafish with ENU and then screened the parthenogenetic offspring of F_1 females for temperature-sensitive defects in caudal fin regeneration. A temperature-sensitive screen was chosen because many of the genes that are involved in regeneration are probably also required for embryogenesis. The mutant they recovered — *nightcap* (*ncp*) — underwent normal fin regeneration at 25 °C but not at 33 °C. At this temperature, fin regeneration stalled two days post-amputation, with the mesenchymal cells that form the proximal part of the blastema showing morphological abnormalities. This part of the blastema — which forms at the wound and from which the new fin arises — is highly proliferative and is believed to drive regeneration.

Through positional cloning, Poss *et al.* next identified the genetic defect that underlies *ncp* — a point mutation in a highly conserved kinase domain of the *mps1* gene. Mps1 is known to function in cell division and in mitotic checkpoint signalling in organisms ranging from yeast to mice. That this mutation underlies the *ncp* mutant phenotype was further strengthened by the authors' findings of mitotic checkpoint defects in *ncp* embryonic cells. Moreover, *mps1* expression is undetectable in adult caudal fins, but becomes upregulated 18–24 hours following fin amputation and soon localizes to a subpopulation of cells in the proximal blastema. Mitotic analyses showed that — two days after amputation — these cells undergo around one-fifth of the number of mitoses in *ncp* mutants as they do in wild-type fin blastemas.

Together, these findings shed new light on the role of the proximal blastema in zebrafish fin regeneration and on the function of *mps1* in the proliferative activity of this tissue. Importantly, they also show the power of zebrafish genetics for investigating the genetic basis of complex tissue regeneration and how conditional zebrafish regeneration mutants can be used to study genes that might also be essential for embryonic development.

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References and links

ORIGINAL RESEARCH PAPER Poss, K. *et al.* Mps1 defines a proximal blastemal proliferative compartment essential for zebrafish fin regeneration. *Development* **129**, 5144–5149 (2002)

WEB SITE

Mark Keating's lab: http://cellbio.med.harvard.edu/faculty/keating/index.html