

No easy answers

Britain's regulator has taken a sensible approach to the fraught question of what kinds of genetic testing should be permitted on embryos.

There is no gene for the human spirit, declared the producers of the 1997 movie *Gattaca*, which related the sobering tale of a eugenic community that had overestimated the usefulness of genes in predicting a person's destiny. The movie's hero, Vincent, overcomes a damning genetic prognosis and resultant discrimination to become an astronaut, while the fall guy, Jerome, fails to achieve the athletic prowess supposedly encoded in his DNA.

Gattaca echoed widespread public disquiet about the possible use and abuse of genetics in the selection of embryos that are free of particular disease-causing genes. Opinions on the matter range from those who think the market should be allowed to determine the use of such testing, as occurs in the United States, to others who would ban embryo selection altogether.

In nations that choose to regulate genetic tests, the real question is how far testing should be allowed to go. They are already used for the genetic mutations that cause cystic fibrosis, where a severely adverse outcome for the child is reasonably certain, and quite early in life. The question now arises of what to do regarding genes (such as *BRCA1*, which leads to breast cancer) where the outcome may not be fatal and comes later. Decisions will soon have to be made regarding tests for genes whose implications are even less specific.

How should societies wrestling with this question proceed? Different nations have sharply different regulatory arrangements, often heavily influenced by their histories of genetics and eugenics. In Germany, for example, an Embryo Protection Law currently prohibits the genetic testing of embryos altogether.

In the United States, by contrast, memories of forced sterilization when eugenics was in fashion early in the twentieth century led to a series of Supreme Court judgements that support the individual's right to procreate. Despite the concerns of some religious groups, this has made the federal government reluctant to restrict such freedom. The result has been a free-for-all that doesn't even offer anxious would-be parents adequate means of assessing the scientific merit of the tests to which they are subjected.

The middle ground is being sought in Britain, where the Human Fertilisation and Embryology Authority (HFEA) regulates both

fertility clinics and embryo research. At a meeting in Belfast last week, the authority ruled that the testing of embryos should be permitted, in certain circumstances, for genes that are not certain to cause severe illness, but merely likely to do so.

The HFEA has a reasonable track record of consulting openly with people of many different backgrounds and views. Its job is to interpret the law in the light of technological developments and take the necessary decisions about what should or should not be permitted. The authority's 18 members represent a mix of scientists, ethicists, law experts, theologians and members of the public. It strives to be independent, and neither its chair nor its deputy chair may be scientists or clinicians involved in fertility treatment.

Last week's decision followed a fact-gathering exercise, publication of a consultation document, a public meeting held last year in London, and consideration of the issue by the authority's ethics and law committee. The HFEA already allowed genetic tests to be used for conditions where a single gene is certain to lead to disease; the new decision extends this to conditions where the gene is only likely to cause disease, and allows affected families and their clinicians to have a say in how severe they consider the disease to be. For the time being, clinics will have to apply to a licence committee for permission to treat each family that approaches them.

The decision could not have pleased everyone, and critics voiced strenuous objections to what they regard as a 'slippery slope' towards the more permissive use of genetic testing. But the decision to allow individual families and their doctors some discretion in determining just what constitutes a serious condition is preferable to the alternative of decreeing prescribed lists of tests that are banned or permitted; the latter path would fall far closer to state-mandated eugenics. The authority should be applauded for finding a middle road that will allow this potentially valuable technology to move forwards, under careful supervision. ■

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Infection biology

Immunology and microbiology come together to fight disease.

It is hardly surprising that scientific papers on human pathogens are often peppered with military analogies. Traditionally, the study of infectious disease has been considered as a conflict in which pathogens are the enemy, to be sought out and destroyed. The

success of antibiotics in the twentieth century reinforced the notion that infectious diseases could be defeated, if only we could find enough ways to kill the microbes that cause them.

Battles still need to be fought, and the report in this issue of the discovery of a potentially new class of antibiotic (see pages 293 and 358) may yield some valuable new weapons. But outright victory looks increasingly unlikely. A surge in strains of resistant bacteria — such as methicillin-resistant *Staphylococcus aureus* (MRSA) — means that an increasing number of bacterial infections cannot be treated effectively. And the growth in the number of emerging

infectious diseases means that the problem is likely to get bigger.

All this is compounded by the withdrawal of many major drug companies from research into antibiotics, and the long timescale for developing new ones (see page 260). Furthermore, persisting in an arms race against microbial resistance may prove futile: it is a race that bacteria are well equipped to win, having evolved mechanisms over millions of years that help them develop resistance to molecules secreted by competing microbes.

Many in the microbiology and immunology communities now believe there is a need for radical new strategies in fighting infectious disease. Developments in immunology and other fields are prompting a convergence towards a more holistic approach that takes into account the complex set of feedback loops between pathogens, host immune systems and our own microbiota.

Better understanding of the host–pathogen interactions at the molecular level may yield answers and open up new ways of thinking about pathogenesis. Rather than always seeking to kill bacteria, for example, molecules that slow their growth or spread may be enough to let the host microbiota and immune system outcompete them, particularly if ways can be found to stimulate or modulate either. Molecules that harnessed our own defences against pathogens would also have the benefit of being less selective for resistance.

Take, for example, *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis. It infects one in ten people in North America

and Western Europe, and one in three worldwide, but only a fraction of these will develop the full-blown disease, with the bacterium dormant or kept in check in the remainder. What tips the balance towards disease? As yet, we have little idea.

Our understanding of the ecology of our own microbiota is limited, as is the molecular basis of host immunity in response to infection. There is still much to understand — until recently, for example, scientists paid little heed to innate immunity, comprising immune cells and secreted molecules that react immediately but rather non-specifically to pathogens. It has only recently been discovered to be much more complex and active than was previously thought.

Such ideas are outlined in an excellent US National Academies report, *Treating Infectious Diseases in a Microbial World* (see <http://fermat.nap.edu/catalog/11471.html>). Infectious diseases have for too long been considered either from the point of view of the microbiologist, with a focus on the pathogen, or from the point of view of the immunologist, with a focus on the host. Basic microbiology, which has lately struggled to win support against competing fields, must not be neglected. But research agencies, universities and scientists should embrace approaches that unite microbiologists and immunologists in the study of infection biology. ■

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Patents for the people

Peer review comes to the patent office.

Great inventions are driven by good science and technology, but great patent applications succeed by exploiting arcane patent law. This is a paradox of the patent system, and is one reason why it is in danger of being overwhelmed by thousands of complex applications, each trying to stake out the biggest possible piece of the intellectual-property pie.

Both the US and European patent organizations are seriously overstretched: the US Patent and Trademark Office (USPTO) says it has more than a million applications in its backlog; and examiners at the European Patent Office in Munich went on strike last week to protest against their workloads.

Also last week, the USPTO held a meeting in Alexandria, Virginia, to examine a novel approach to the problem. The Community Patent Review project (<http://dotank.nyls.edu/communitypatent>) tries to place the patent process firmly back in the hands of scientists and engineers by asking them for feedback on pending applications.

Under the proposed system, researchers would volunteer to be informed whenever patent applications in their areas of expertise are published. They could then use an electronic bulletin-board to post any prior publications that might be relevant. They could also rank other postings in order of interest. Ideally, the result would be a well-ordered list of publications that the patent examiner could use to determine whether the application is truly innovative.

The idea was the brainchild of Beth Noveck of New York Law School and has won forthright backing from IBM. The computer

corporation, which obtains more patents than any other company, says its support is part of a broader push for patent reform. Now the USPTO is pondering a pilot project of the idea. IBM would volunteer some of its own applications for initial review.

Unsurprisingly, perhaps, some of the patent lawyers who attended the USPTO meeting were unimpressed with the idea. They pointed out grounds for legal challenges to the result of the suggested process: if patent examiners ignored some of the comments they received, for example, they might be accused of “inequitable conduct”, which in turn might invalidate the patent. Additionally, comments posted on the site could run foul of current law, which limits communication between patent examiners and outside sources while an application is under review.

Then there is the question of who would bother to participate in the process. For the most part, researchers take part in scientific peer review because the community expects it. No one expects anyone to review patents, and it is conceivable that the only people who come to the site would be rival companies, their lawyers, and cranky ‘inventors’ hocking cold-fusion reactors and perpetual-motion machines.

But similar pitfalls have not entirely undermined ‘open’ review systems in other spheres, and the USPTO should at least give the idea a try. Scientific peer review is often credited with keeping research honest, and patent peer review may be able to clean up some of the spurious claims of those looking to profit from vaguely worded applications. And even if it fails, the pilot could assist in the search for fresh approaches for dealing with the backlog. ■

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