research, it may not matter that the damage or symptoms in the model developed by a different pathway to that which occurs in patients — orthopaedic injuries are one example. But in other areas, such as epidemiology, it matters a great deal.

Recognizing that standard models have limitations does not mean we should give them up. Rather, we should deliberately account for their limitations as part of study design — for example, by analysing the role of a gene in mouse strains with different genetic backgrounds. No single species, no matter how highly engineered, can ever serve as a universal model: every species has unique features that may be assets or faults, depending on the question being asked. For instance, the lack of developmental plasticity in *Drosophila* and of genetic variability in inbred rats limit what these models can tell us about ecological effects on development, but make them powerful tools for studying gene function during development.

We also need to broaden our range of models to include species such as Antarctic icefish, comb jellies, cichlids, dune mice and finches that are naturally endowed by evolution with features relevant to human diseases[10]. Studying the basis of unique adaptive traits in these animals may yield insight into human disorders such as osteoporosis, cataracts and cancer.

Immediately and practically, the US National Center for Advancing Translational Sciences in Bethesda, Maryland, should support the development of new systems for investigating problems that are not tractable in currently favoured models. It should also fund investigations into fundamental questions about model-based research (see 'Choosing the right candidate'). The resulting insights would help scientists to select the best models for advancing basic and applied research, and strengthen the bridges between them. ■

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J. REED/REUTERS/CORBIS

Pro-choice and pro-life activists clash outside the US Supreme Court in Washington DC.

Politics and fetal diagnostics collide

Without better regulation, non-invasive prenatal genetic tests will be targeted by US anti-abortion lobbyists, argues **Jaime S. King**.

In the United States, pro-life advocacy groups, notably Americans United for Life, based in Washington DC, have been making headway in their mission[1] to limit women's access to abortions "state by state, law by law and person by person". In 2011, 24 US states enacted 92 new provisions restricting abortion — nearly triple the previous record of 34 in 2005 (see 'Clamping down'). One of the strategies of pro-life advocates is to target the reasons for which a woman can have an abortion. Meanwhile, a major development in prenatal care, called non-invasive prenatal genetic testing (NIPT), promises to increase the genetic information available to women early during their pregnancy.

The US Food and Drug Administration (FDA) cannot control how people use information from genetic tests. But by developing a clear regulatory framework for NIPT and improving public understanding of NIPT's benefits and limitations, the agency could help to allay fears that the tests will lead to a drastic increase in selective abortions.

NIPT has the potential to improve women's reproductive autonomy. But if it is not integrated cautiously into prenatal care, the technology could be targeted to support burgeoning strategies to restrict abortion.

In recent years, two blood tests combined with an ultrasound have been the most common method for determining a fetus's risk of having a congenital disease such as Down's syndrome. Results from this type ▶

of test are available only at the beginning of the second trimester. A woman can then choose to schedule an amniocentesis, a more accurate but more invasive test. For this, a clinician inserts a needle into her abdomen to extract a sample of amniotic fluid, which contains the fetal cells needed for genetic testing. The procedure increases the risk of miscarriage by around 1%.

Instead, by analysing fragments of fetal DNA in a pregnant woman's blood, NIPT can reveal potential problems without physical risk. Offered when a fetus is just ten weeks old, NIPT gives a woman much more time to have genetic counselling and confirmatory tests, and to make a reasoned decision about whether to have an abortion while it is still legal for her to do so (in most US states, only before the fetus is 24 weeks old)[2].

NIPT is now used to determine a fetus's blood type, sex and father, and to screen for chromosomal disorders such as Down's syndrome and trisomy 18. The technique is not yet offered commercially for single-gene conditions such as Tay-Sachs disease and cystic fibrosis, but it probably will be soon. Even the use of NIPT to reveal whole fetal genomes may not be far off. In June, researchers sequenced an entire fetal genome from a maternal blood sample[3], and another group did the same a month later[4].

RIGHTS AND REGULATIONS

In the United States, NIPT is emerging just as several states have begun to restrict women's access to abortions sought for certain reasons. In March, a Missouri state representative introduced the Abortion Ban For Sex Selection and Genetic Abnormalities Act of 2012. If this bill were to become law, it would prohibit doctors from carrying out abortions that they knew were being sought because of the fetus's sex or because the fetus had been "diagnosed with either a genetic abnormality or a potential for a genetic abnormality"[5].

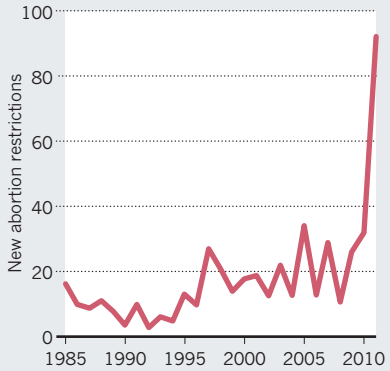
"The FDA still has not developed a comprehensive regulatory scheme for genetic tests."

Abortions sought because of a fetus's sex are now banned in four states, and bans have been proposed in six others. In May, a bill that would ban all US providers from knowingly performing abortions sought because of the sex or race of the fetus nearly won the two-thirds majority needed, under 'fast-track' rules, to pass the US House of Representatives. Two weeks later, a similar bill, focused on 'sex selection' only, was presented to the US Senate. If it wins majorities there and in the House, it will be sent to the president, whose signature would make it national law.

As the use of NIPT becomes more widespread, pro-life advocates will almost certainly see the technology as a reason to further constrain women's abortion rights. In June, the *National Catholic Register* wrote that pro-lifers view NIPT as "an enhanced 'search and destroy' diagnostic tool" that will drastically increase the number of abortions[6]. Even in Europe, where abortion has historically been a less divisive issue, the technology has prompted anger from various groups. In June, two months before the life-sciences company LifeCodexx, based in Konstanz, Germany, made its PrenaTest for Down's syndrome commercially available, 30 Down's syndrome organizations from 16 countries formally objected to the sale of the test in the European Court of Human Rights.

CLAMPING DOWN

The number of provisions restricting abortions in US states has risen sharply in recent years.



SOURCE: GUTTMACHER INST.

Ideally, no fetus would ever be aborted because of its sex or skin colour. And it is hard to argue that allowing parents to check for hundreds or thousands of traits with one blood test will not facilitate abortions based on societal or individual prejudice. After all, in Asia, there are 160 million fewer girls and women than normal live-birth sex ratios would predict, partly because of the widespread use of ultrasound over the past two decades[7].

But forcing women to have children they do not want will not end prejudice. Instead, it will create a slew of problems. Greater restrictions on abortion may result in more suffering for children[8]. Bills restricting terminations sought for particular reasons will drive a wedge between patients and providers. They will encourage women to withhold information or lie, and they will punish providers serving clients who tell them the truth. Moreover, by dictating which fetuses can legally be aborted, states are entering the dangerous territory of valuing some lives more than others.

US companies that sell NIPT products (such as the California-based firms Sequenom in San Diego, Verinata Health in Redwood City and Ariosa Diagnostics in San Jose) are being cautious. They offer tests only through physicians and for a few conditions, and advertise them as 'screening tests' that may require follow-up procedures. Yet there is too much money to be made from a 'risk-free', relatively inexpensive prenatal genetic test for this restrained approach to last. Worldwide, nearly 50 companies are now developing NIPT products.

HANDLE WITH CARE

The FDA must step up its involvement to ensure that NIPT is integrated into prenatal care carefully — and, especially, to prevent it from being offered directly to consumers, as are other genetic tests.

The FDA still has not developed a comprehensive regulatory scheme for genetic tests, despite repeated calls to do so from government advisory groups (such as the US Secretary's Advisory Committee on Genetics, Health and Society) and non-profit organizations (such as the Genetics and Public Policy Center in Washington DC). This regulatory vacuum is especially problematic in the prenatal context, in which test results can affect parents' decisions to terminate or continue a pregnancy.

The FDA urgently needs to develop a regulatory framework that would allow parents to use prenatal genetic tests under the guidance of a physician and within some general boundaries. As a starting point, the FDA should specify the degree of accuracy and clinical utility required for companies to market a prenatal genetic test. It should also help physicians, pregnant women and the general public to understand the risks, benefits and limitations of such tests — by working with biotechnology companies offering NIPT products, professional societies such as the American Academy of Pediatrics and patient advocacy groups such as the National Down Syndrome Congress.

Abortion has always been a charged issue in the United States. Against this backdrop, NIPT must be handled with care. ■

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