Meet your unborn child – before it's conceived

Virtual embryos will allow parents to screen out genetic disorders

Catherine de Lange

WILL my baby be healthy? It's a question that concerns every prospective parent. Now a service that creates digital embryos by virtually mixing two people's DNA will give a clearer glimpse of their possible child's health, and perhaps much more – before it has been conceived.

The Matchright technology will be available in two US fertility clinics later this month, allowing people to screen out sperm donors who, when their genes are combined with those of the intended mother, could increase the risk of a child inheriting genetic diseases. The company that markets the technology, GenePeeks, hopes to expand worldwide.

But the technology's patent also includes a list of traits that aren't necessarily related to health – such as eye and skin pigmentation, height and waist size – raising concerns that it could be used to select embryos on the basis of more superficial characteristics. "It covers any disease or any trait that has a genetic influence," says Lee Silver at Princeton University, who co-founded GenePeeks – even those where the genetic basis has yet to be discovered.

"Eventually screening of virtual embryos will be open to any couple hoping to conceive naturally"

To find out how the technology may affect parents' future choices, *New Scientist* sent the patent to people working in reproductive health.

The priority should be medical problems, says Martina Cornel of the European Society of Human Genetics. This is what GenePeeks plans to do. It intends to use the system to identify rare conditions such as cystic fibrosis and Tay-Sachs disease, which are passed on to a child when both parents carry a mutation in a single gene.

Screening for genetic disorders usually involves sequencing the DNA of the prospective parents. GenePeeks takes this a step further: algorithms are fed this information and use it to digitally recreate the process of genetic recombination – the mixing of genetic information between a sperm and an egg. This allows them to look at the genetic make-up of the possible embryos.

Before a woman selects a donor from a participating fertility clinic, the Matchright algorithms, which Silver developed, are run thousands of times for each donor. This produces up to 10,000 simulated embryos per pairing. These are sequenced to look for mutations in single genes that can cause some 500 rare diseases, and then used to work out the disease risk in the hypothetical child that would develop from that particular partnership. The woman, who pays $1995 for the service, then gets a list of "safer" donors from which to choose.

To know which mutations to look for, the software searches databases of genes linked to different conditions. To validate the method, the company used the software to digitally pair anonymous men and women whose genomes were sequenced as part of the 1000 Genomes Project. GenePeeks then screened their virtual embryos and compared the incidence of predicated disease to that in the general population.

"These studies confirmed the system's ability to accurately predict a future child's risk profile," says co-founder Anne Morriss. However, only when a critical mass of children are born using the system will its true power become apparent. And even then it's still a game of probabilities – you might shift the likelihood of passing on traits by screening out certain donors, but it doesn't rule out the effect of spontaneous mutations that might arise during development.

Complex disorders

Most IVF clinics already test donors for about a dozen genetic disorders arising from single gene mutations, says Geeta Nargund, a fertility consultant at the Create Fertility clinic in London. They also take a family history and carry out general health checks.

The new technique will screen for more diseases, which everyone *New Scientist* spoke to agreed could be a lifesaver. "[These disorders] can be catastrophic not only for the child but also for the family," says Dagan Wells at the University of Oxford.

But diseases caused by mutations to a single gene only affect 4 per cent of the population. Next, GenePeeks says it would like to use the software to screen for complex disorders that are affected by clusters of genes, such as schizophrenia, or complex diseases with a genetic basis, such as breast cancer.

Such conditions will be harder to predict, says Wells. "We don't always have a good understanding of how all these genes interact. And some are modified significantly by the environment."

Eventually the company would also like to offer the technology to couples hoping to conceive naturally, says Morriss. This means they could analyse their disease risk and make more

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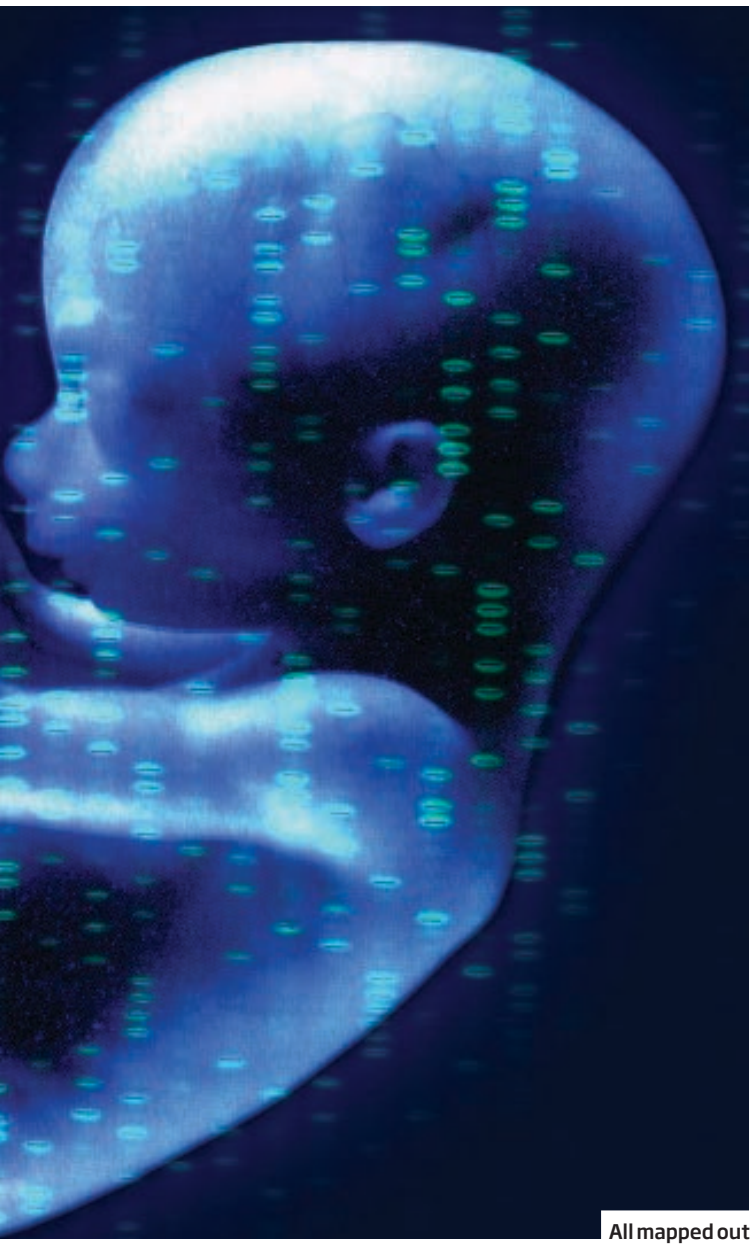

All mapped out

informed decisions about their future, she says. The patent also includes the possibility it could be used by those sizing up potential partners on dating sites.

These intentions, coupled with the long list of traits on the patent, (see "What's on the list", right), rung alarm bells with some of the scientists we spoke to.

Whether or not the technology works for the more complex conditions and traits, the concern is that practices like this will change people's expectations about being able to select traits in their future children, says Marcy Darnovsky of the non-profit Center for Genetics and Society in Berkley, California. "It has the potential to change people's experience of what it means to be a parent."

"The technology has the potential to change the experience of what it means to be a parent"

But Hank Greely, a biomedical ethics specialist at Stanford Law School points out that just because certain traits are in the patent doesn't mean they will be used. Indeed, Morriss is adamant that the firm doesn't intend to use the system for non-medical purposes.

Last year, a similar patent was granted to personal genetics company 23andMe for their "inheritance calculator" – software that allows couples to see the traits they might pass on to their children. The patent specifically mentioned it could be used in fertility clinics to allow clients to select for certain non-medical traits in their donors. After a strong backlash, 23andMe stated it wouldn't be used in such circumstances.

However, there are situations where it might be helpful for parents to select certain physical traits. "It may be in the interest of the future child to resemble its social parents," Cornel says. For example, one part of the patent describes how the technology might be used by infertile or gay couples to get an idea of the traits their genetic children would have, allowing them to select a donor that produced the closest match.

"Where it is more ethically challenging is when you expand beyond couples in desperate need for a donor, to couples that are just interested in more trivial things," says Wells.

Silver says that what the patent is used for in future will be a business decision. He also says that owning the patent means the firm can prevent others from using the technology in unintended ways.

"This is such a sensitive issue because we are on the cusp of being able to do very extreme things with the biological knowledge that is being developed," says Darnovsky. "It is important that people understand what the technical possibilities are."

Because the simulated embryos are a new concept, it's not yet clear who will regulate the technology. "There need to be processes and specialists who can deal with it," says Nargund. Whatever happens, Darnovsky believes that the future of the technology should be open for discussion: "It depends a lot on how we approach it from a social perspective. If we want to go down that road we could find ourselves with new inequalities that are written into the genome." ■

WHAT'S ON THE LIST

Here is a selection of the traits included on GenePeeks's patent. Anne Morriss, co-founder of the company, says the traits included were drawn up from pre-existing lists of components included in medical exams

RARE SINGLE GENE DISORDERS
Tay-Sachs disease
Muscle-eye-brain disease
Zellweger syndrome
Bloom syndrome
MCAD deficiency

COMPLEX DISORDERS
Epilepsy
Alzheimer's disease
Diabetes, types 1 and 2
Breast cancer
Prostate cancer
Stroke
Asthma

BEHAVIOUR
Mental stability
Cognitive ability
Neuroticism
Nicotine dependence
Propensity to cross the right thumb over the left when clasping hands
Episodic memory
Sleep pattern

APPEARANCE
Eye and skin pigmentation
Breast size
Dimples
Eyebrow shape
Widow's peak
Height