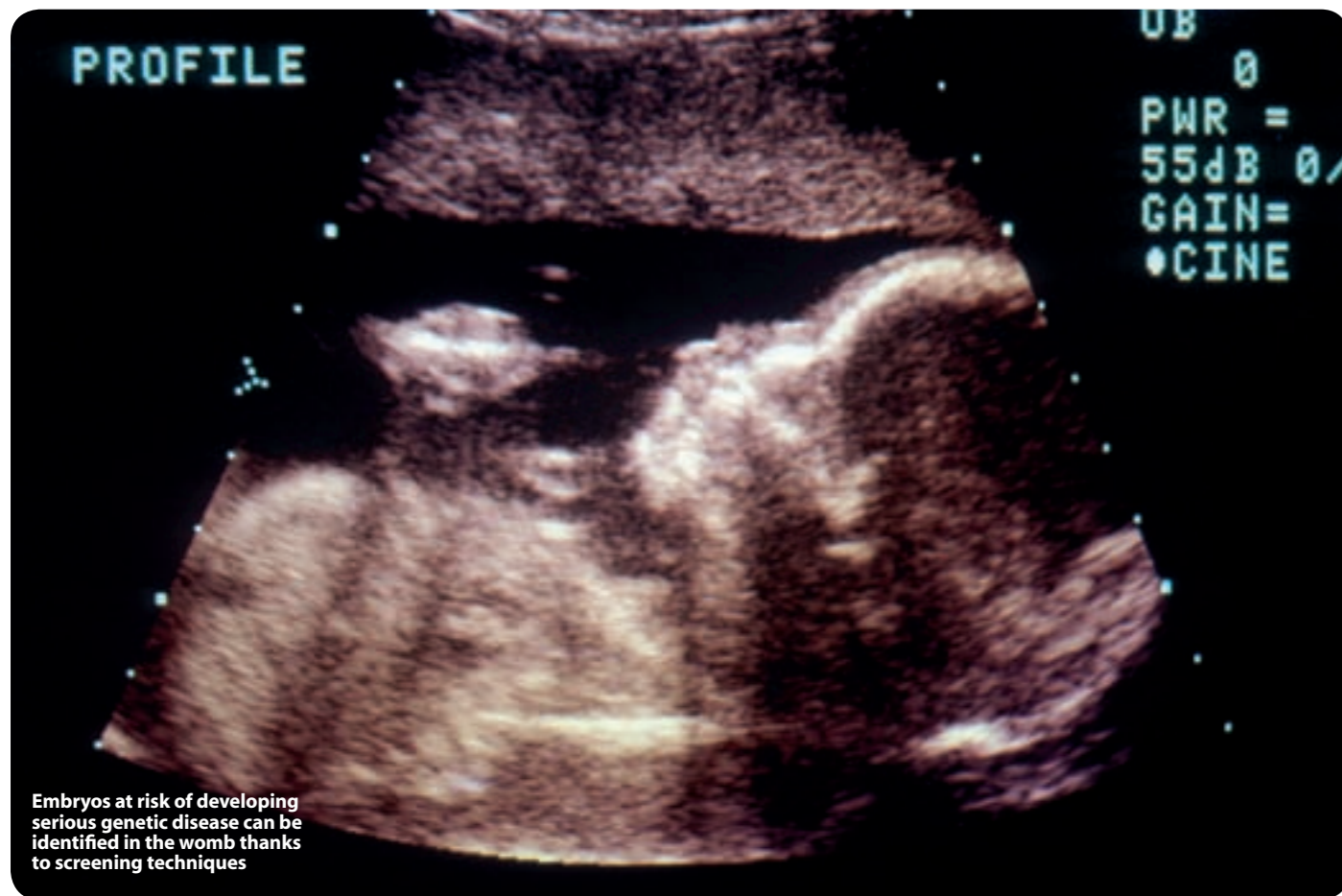


# Gene genius

Beyond outraged tabloid headlines about genetic manipulation, medical research teams are pioneering developments that could save people from inheriting muscular dystrophy



Embryos at risk of developing serious genetic disease can be identified in the womb thanks to screening techniques

**D**esigner babies is the medical ethics dilemma of our era, generating passionate debate and hyperventilated headlines on both sides of the argument. But while most of us are concerned at the prospect of parents being able to order the sex of their baby, not to mention its eye or hair colour, most people would admit that advances in genetics could be the answer to many parents' prayers – especially those who have genetic illnesses in their family.

Take the ground-breaking work being done by Mary Herbert, Reader in Reproductive Biology and Doug Turnbull, Professor of Neurology at Newcastle University. Their team is working on a technique called nuclear transfer, which could help prevent mothers from passing on inherited mitochondrial diseases to their unborn babies. Mitochondrial myopathies belong to this group of disorders and they can be caused by a mutation in the DNA of mitochondria. Mitochondria are the

**'The more embryos we have, the more likely we are to have one good enough for a pregnancy'**

powerhouses of the cells and convert the food we eat into energy. The mitochondrial genome contains a very small number of genes, but if it gets damaged it can lead to severe diseases. Mitochondrial myopathies primarily affect the muscles, and sometimes other parts of the body. Unfortunately there is currently no treatment.

'Mitochondrial DNA is passed down only by the mother and, because of the way it is inherited, genetic counselling and prenatal diagnosis sometimes can offer only limited

advice for affected families,' explains Dr Marita Pohlschmidt, Director of Research at Muscular Dystrophy Campaign.

Dr Herbert and Professor Turnbull's research, which is funded by the Muscular Dystrophy Campaign and approved by the Human Fertilisation and Embryology Authority, hopes to determine whether mitochondrial disease can be prevented by removing the healthy pronucleus (the structure within a cell that contains most of the genetic material) from a fertilised egg that contains bad mitochondria and putting it into an egg from a donor that contains only good mitochondria. Research on mice has been successful – now Professor Turnbull hopes to discover whether the same techniques can be adapted to humans.

'The research will enable us to see whether this technique can prevent transmission of mitochondrial disease, but we're still at least five to 10 years away from it being a reality,' he says.

But the technique has received criticism.

Although Professor Turnbull's research only tackles the feasibility and safety of pronuclear transfer, his critics are concerned about the use of genetic material from two women, saying that any child born using this technique would effectively have two mothers.

Dr Pohlschmidt says: 'But what should be kept in mind is that the mitochondrial DNA only carries a small number of genes and more than 99% of all genes are localised in the nucleus. And if the research proves the technique is a success, it could give families with the disease more freedom and the choice of having a healthy child.'

## Screening for genes

Another technique that has recently come to prominence is a breakthrough in pre-implantation genetic diagnosis. PGD has been used for several years to test embryos for serious genetic disorders, but its application has been limited. It can be used for couples who opt for IVF where you take eggs from the mother, fertilise them with the father's sperm, then test cells from the resulting embryos and only reimplant one which does not carry the genetic mutation tested for. For example, if you, your partner or both carry a mutated gene in your family and risk passing it on to your children, PGD techniques might enable you to screen out



New genetic testing techniques mean three out of four embryos may be suitable for IVF transfer

those embryos that have inherited the genetic defect and thereby find for a pregnancy an embryo that will not develop the disease.

Professor Peter Braude and his team at the Centre for Pre-implantation Genetic Diagnosis (PGD) at Guy's and St Thomas' NHS Foundation Trust have announced their use of a new PGD technique, pre-implantation genetic halotyping (PGH), which makes PGD more accurate.

'PGH will make a big difference for some patients,' says Professor Braude, who explains that, for Duchenne muscular dystrophy, previously PGD could only determine the sex of the embryos, making sure only unaffected female embryos were used.

'Now with PGH, we will be able to detect unaffected males as well as test for a much larger range of these diseases.'

'This means that instead of the proportion of embryos expected suitable for transfer being 50:50, we can now expect it to be 75:25 – that is, three out of four being available for transfer. And the more embryos we have available, the more likely we are to have one that is of suitable quality and likely to produce a pregnancy.'

Currently, PGH can be offered to those parents at risk of passing on Duchenne muscular dystrophy, Spinal Muscular Atrophy and myotonic dystrophy or genetic conditions such as cystic fibrosis, Huntington's disease and Prader-Willi Syndrome, although more diseases are expected to be added to the list soon.

Professor Braude's team has been using PGH since March and, at the time of writing, had already used it to achieve five pregnancies.

The technique will not be suitable for all people, because in some families the genetic disorder has arisen spontaneously. Using this technique also requires testing other family members. It is therefore crucial that families who are interested in this technique make early contact with a Medical Genetics Department, well before a pregnancy is planned, so that all the necessary preparatory investigations can be done in good time.

• Many thanks to GlaxoSmithKline, which has recently agreed to fund Professor Turnbull's work for three years.

## Did you know that...

The Muscular Dystrophy Campaign is at the front of the fight against muscle disease in the UK and this is strongly reflected in our research programme. Since the charity was founded 48 years ago, we have raised and invested more than £50m into research.

We provide salaries and equipment for top quality scientists at universities in Scotland, England and Wales for projects running for a maximum of three years. Research grant applications undergo a rigorous peer review process involving international experts and only the best science will be funded.

There are currently 23 live research projects, costing over £1.2m a year, covering 12 different muscle conditions. The studies investigate the molecular causes for disorders such as myotonic dystrophy, congenital muscular dystrophy, myasthenia gravis and spinal muscular atrophy.

The knowledge gained from these studies is essential to drive research that can lead to new avenues for treatment.

And the charity's investment into research

is already crowned with success. Professor Kay Davies, who has a longstanding history of support with the charity, was able to co-found a company to further her promising approach to treat Duchenne. In the future the technique might be transferred into a clinical trial.

Meanwhile, Professor David Rubinsztein is investigating a pharmacological approach to treating oculopharyngeal muscular dystrophy. The promising first results were published at the beginning of this year and he was invited to present his data at an international congress in July in Istanbul (see page 4).

Other projects include two exciting clinical pilot studies into disease management for people with Charcot-Marie-Tooth disease and mitochondrial myopathies. Both look closely at the needs of patients and will have a direct impact on their quality of life.

To find out more about any of the projects or contribute funds towards our research, visit us online at [www.muscular-dystrophy.org/research](http://www.muscular-dystrophy.org/research), email [research@muscular-dystrophy.org](mailto:research@muscular-dystrophy.org), or call 020 7720 8055.

**'If nuclear transfer is a success, it could give families with the disease more freedom and the choice of having a healthy child'**



## Get in touch

If you have any questions about any of our many current research projects, contact Dr Marita Pohlschmidt, Director of Research.

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