

TECHNOLOGY » Stem cell research

No 'voodoo magic'. But maybe a miracle

The biotech industry may not have woken up to it yet, but a Saudi doctor's accidental discovery could herald a new future for one of medical science's most controversial breakthroughs.
Maggie Lee reports



Hope comes out of a test tube: Dr Ilham Abuljadayel on a hospital ward in Mumbai. Her work could quell ethical concerns about stem cell research by offering an alternative to using human embryonic cells (below)

SWAPAN PAREKH; EPA

Stem cell research has become a much talked of issue in the US election. Coming out against President George Bush's policy on the issue have been people such as the Hollywood actor Michael J Fox, a Parkinson's disease sufferer, and the widow of the paralysed *Superman* star Christopher Reeve.

But now a London-based biotech company says it can take an adult human cell from a patient and use it to create a stem cell. If ongoing medical trials being conducted in India to substantiate these claims prove successful, the whole issue will be turned on its head.

TriStem's discovery challenges the current scientific orthodoxy that it is not possible to return a mature cell to its former evolutionary state as a stem cell. If fully validated, it will have profound implications for the treatment of patients suffering from a wide range of diseases that mainstream stem cell researchers are currently tackling. These include leukaemia, heart disease, Type 1 diabetes and spinal cord injury.

Stem cells are therapeutically valuable because of their ability to replicate indefinitely and become a production line for the replacement of damaged specialised cells. But research in this field is controversial. As stem cells have until now generally been harvested from embryos or foetal sources, research often raises complex ethical issues. It has also polarised political opinion, not least on the campaign trail leading up to this week's presidential election.

The application of TriStem's technology neatly side-steps these difficulties. It may provide

a route to creating stem cells that is an alternative to harvesting cells from embryos or foetuses, so making research less expensive, risky and controversial.

With roots in Britain, Dublin and Saudi Arabia, TriStem was founded in the late 1990s by Ilham Abuljadayel, a Saudi Arabian doctor, and her UK-resident husband, Ghazi Dhoot. Their aim is to exploit patents they registered earlier in the Nineties, following Dr Abuljadayel's ground-breaking, but sceptically reported, discovery about the creation of stem cells.

Her breakthrough came by accident when, while working as a consultant immunologist in Jeddah, she forgot to add an ingredient to a mixture she was using to kill leukaemia cells. Instead of dying, the cells were transformed into stem cells.

"It was such a rare occurrence, it was as if ET had landed," Dr Abuljadayel says. She

successively repeated the process, which she later named "retrodifferentiation", to verify the results, and patented it at the suggestion of her husband.

"It was as if the cells had acted like a VCR and wound themselves back to the beginning," she continues. "It was extraor-

'If mature cells can become stem cells, a patient's own cells can be used to treat a disease'

inary. I realised that if mature cells can be flexible to become stem cells, then a patient's own cells could be treated to be used to treat disease."

Money was then needed to fund research and support clin-

ical trials. Philosophical about the lack of venture funding, particularly after the downturn in world stock markets in 2001, her husband used his well-honed skills as a former investment banker working in American and Arab institutions to raise private equity. He and his wife have also invested in the business themselves.

Initially, TriStem had envisaged carrying out clinical trials in the UK. However, after fruitful discussions with the Indian Council of Medical Research, the work went ahead instead in Mumbai. Trials were conducted with patients suffering from aplastic anaemia, a life-threatening condition more common in developing countries than in the West. Sufferers' bone marrow is damaged, causing inadequate production of normal blood cells and platelets; without regular blood transfusions, aplastic anaemia is fatal.

Under trial conditions TriStem separated the patients' immune cells and treated them with the antibody for about two and a half hours. The patient's treated cells were then reinjected.

Dr Abuljadayel was amazed by the results. "When the patients' bone marrow was analysed you could see evidence of regeneration. Some of these people were taking 12 units of blood transfusions every month. Now some of them are transfusion independent. They haven't had any transfusions since the stem cells created from their own cells were injected," she says.

Aware of the scepticism surrounding her research (one critic accused TriStem of performing voodoo magic), Dr Abuljadayel was happy to be

accompanied in Mumbai by independent expert witnesses and a television production company.

Aside from having the obvious benefits for patients who in some cases had little hope of living much longer, the cost savings Dr Abuljadayel's work has opened up potentially huge new revenue opportunities in the treatment of diseases that rely heavily on blood products. TriStem has, over the past two years, been developing a prototype machine for clinical use that will convert a patient's adult cells into stem cells for specific therapeutic treatments. The manufacturing and distribution of this device will be outsourced, with TriStem retaining ownership of the software that both drives and audits the retrodifferentiation process. Commercially, this could deliver a huge bonanza for investors.

Dr Tim McCaffrey, a stem cell expert at the George Washington University in Washington DC, can vouch for TriStem's research. A self-confessed "conservative person - not prone to run with wild hares", he jointly published research with Dr Abuljadayel this year. The hypothesis that a cell can reverse its differentiation programme is not a new one, he says, but there have been problems in proving this thesis. "You need to see it to believe it, and no one has been able to create and demonstrate these conditions before."

He finds scientific scepticism ironic, given the lack of evidence supporting claims that cells *cannot* reverse their nature. "Just because someone hasn't done it, doesn't mean it can't be done." For Dr McCaffrey, the scepticism surrounding the

discovery is reminiscent of the problems encountered by Dr Stanley Prusiner, winner of the 1997 Nobel Prize for medicine, in getting his once-heretical prion theory accepted. (Prusiner discovered that proteins he named prions can infect human beings and are implicated in dementia-related conditions such as Creutzfeldt-Jakob disease.)

Mr Dhoot is aware of another company using adult cells in the same manner for trials on humans. But he believes TriStem remains unique. Not only is it the one company that possesses the retrodifferentiation technology, it has also conducted clinical trials on a stand-alone basis (ie, independent of any other treatment or therapy).

Over the next two years, Mr Dhoot envisages that the company will probably focus on developing treatments for leukaemia, spinal cord injuries, Type 1 diabetes and heart disease.

He remains pragmatic about the academic world's relative silence and is confident he can raise further private equity, being in no hurry to take the company public. He is equally clear that, at some point, a portion of either the company's future earnings or shareholding will be used for charitable purposes.

When pressed about his worst moments, Mr Dhoot says that, as with any start-up or developing enterprise, these have been too numerous to list. However, he and his wife are unequivocal in recalling their proudest moment. It occurred when one of the patients in the Mumbai trial gave Dr Abuljadayel a small present. Turning to her husband, Dr Abuljadayel said: "This is my Nobel Prize."

