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## BMJ INVESTIGATION

# Cord blood banking: Experts raise concern over claims made for stem cell applications

Marketing by some private biobanks may be misleading expectant parents about the procedure's value, writes **Jacklin Kwan**

Jacklin Kwan *freelance journalist*

Umbilical cord blood banking has gained prominence in the past decade as an option for expectant parents worried about their child's future health.<sup>1</sup> Parents pay private biobank companies up to £3000 (excluding annual storage fees) to freeze their baby's cord blood, which contains stem cells, in case the infant develops a condition that could be treated with stem cell therapy.

Cells4Life, which claims to be the UK's largest private biobank for cord blood banking, says that its particular method delivers more stem cells from umbilical cord blood than its competitors' processes. For this marketing message it relies on research published in the *Journal of Stem Cells Research, Development & Therapy*. Publication of this research took place just 17 days after receipt of the manuscript, a timescale far shorter than is typical for peer reviewed journals. Two editors listed on the journal's editorial board say they did not in fact hold these roles, *The BMJ* discovered (box 1).

### Box 1: Claim of superior technology by UK's largest private biobank raises questions

Cells4Life says it is the UK's largest provider of cord blood banking services. The firm markets its proprietary technology TotiCyte—a “precise, low concentration mixture of two solutions,” the cryoprotectants dimethyl sulfoxide (DMSO) and dextran—as the reason why, after collection, processing and freezing, its samples have three times as many stem cells as competitors that use other processing methods (assuming that freezing and collection are kept the same across all methods).

Patricia Murray, professor of stem cells and regenerative medicine at the University of Liverpool, says that there is no clear scientific reason why TotiCyte should outperform market alternatives. “All they've got in TotiCyte is DMSO and dextran, which are well established cryoprotectants,” she said, “There may just be a slight difference in the percentages of DMSO and dextran, but you wouldn't expect it to have such a dramatic effect on cell survival.”

Responding to this, Cells4Life's chief executive, Claudia Rees, says that TotiCyte is used as a blood separation reagent to sediment red blood cells so they can be removed before freezing, not as a cryoprotectant.

Murray points to a written opinion by an international searching authority (ISA or patent office) in 2014 when Cells4Life applied for a patent under the World Intellectual Property Organisation. The ISA examined TotiCyte's application to sediment red blood cells as well as its role as a cryoprotectant and concluded: “It follows that the addition of DMSO to the dextran composition does not add any technical effect in the use and method for white blood cell enrichment and appears merely to

serve as a patent strategical means to establish novelty over the art.”

Rees told *The BMJ* that Cells4Life has been granted patents in the US and China for TotiCyte as proof of its novelty.

### Published research claims

The evidence for Cells4Life's TotiCyte claim is given in a “peer reviewed publication,” the *Journal of Stem Cells Research, Development & Therapy*, published by Herald Scholarly Open Access. The research article referenced by Cells4Life was received on 14 May 2021 and published only 17 days later.<sup>2</sup> When asked by *The BMJ*, the journal in question claims to maintain a double blind process of peer review.

However, a 2017 study of journal response times suggests that journals typically take 12-14 weeks to handle accepted medicine and public health papers.<sup>3</sup> This is the time in which the paper is under the responsibility of the journal—in other words, the time it takes for the journal to evaluate the manuscripts, find reviewers, have time for the reviewers to complete their work, and for editors to evaluate manuscripts on the basis of reviewers' reports. It does not include the time taken for authors to revise and resubmit their work.

*The BMJ* contacted two editors who were listed on the journal's editorial board. One said that they had “never held an active role in the journal nor received any articles or communications from them for review or any other purpose.” The other said that they “never accepted the position of editor to this journal.”

After being contacted by *The BMJ*, both researchers have asked the *Journal of Stem Cells Research, Development & Therapy* to remove their names. *The BMJ* was unable to make contact with the journal about this matter.

Rees says, “The *Journal of Stem Cells Research, Development & Therapy* has its own independent editorial board, provides an NLM [National Library of Medicine] identifier [and] an impact factor, and operates under the COPE guidelines.” COPE is the Committee of Publication Ethics, a non-profit organisation that promotes and defines best practices in scholarly publishing.

Experts in regenerative medicine have criticised Cells4Life's marketing directed at expectant parents, which they say contains misleading statements. Charles Murry, director of the Institute for Stem Cell and Regenerative Medicine at the University of Washington, Seattle, says claims that stem cells can develop into almost any type of cell in the body have been “very rigorously disproven.”

## “Routinely used” and promising—or “rigorously disproven”?

Depending on the specific company and on whether parents choose also to bank cord tissue, private umbilical cord blood banking services range from £550 to around £3000, excluding annual storage fees of over £100 to keep samples frozen. Those financial costs are often marketed as an investment, given that there have been promising reports of successful use of stem cell based therapies to treat a wide range of potentially life threatening diseases, from cerebral palsy to leukaemia.<sup>4,5</sup>

The Cells4Life website claims that “umbilical cord blood is routinely used in treatments for over 80 different conditions and diseases,” including cancers, blood disorders, immune disorders, and autism. It says, “Umbilical cord blood stem cells are pure and plastic, meaning that they can become almost any cell in the human body,” and, “They can become almost any tissue type in the body and may even be used to regrow entire organs.”

But Murry says this list of applications is unrealistic. “There were people making these claims in the late 1990s—that these cells have the plasticity to become other things—but that’s been very rigorously disproven.”<sup>6-8</sup> He tells *The BMJ* that the haematopoietic stem cells (HSCs) and mesenchymal stem or stromal cells (MSCs) harvested from cord blood (box 2) are a form of adult stem cell and that there is a “restricted repertoire” of what they’re able to develop into—namely, blood cells for HSCs and connective tissue cells for MSCs.

### Box 2: What is cord blood banking?

Blood in the umbilical cord contains haematopoietic stem cells, which can be used to develop into different kinds of blood cells (such as red blood cells), and mesenchymal stem cells (stromal cells), which are important for repairing some body tissues. After birth, the umbilical cord can be clamped and the blood within it and the placenta cryogenically stored. According to the Human Tissue Authority, 376 843 units of cord blood were stored with the UK’s private cord blood biobanks at the end of 2022, representing over 90% of the country’s total stores of cord blood supply. The remainder is stored in philanthropic umbilical cord blood banks, such as the independent charity Anthony Nolan,<sup>9</sup> to which parents can choose to donate cord blood for other patients or research.

Stem cell therapies are showing promise in treating some conditions that diminish quality of life, such as cerebral palsy.<sup>4</sup> Finding a stem cell match through public banks or within families can be a challenge.

Responding to this criticism, Cells4Life says, “Any cursory search of published literature on future applications of perinatal stem cells demonstrates the huge potential that cord blood holds for use in regenerative medicine in the future.” It references papers in which MSCs are used to reduce inflammatory immune responses after organ transplantations and adds: “MSCs can be transformed into inducible pluripotent stem cells (iPSCs). This technology allows a cell to mimic an embryonic stem cell ... capable of forming any tissue with [the] exception of germ cells.”

## Potentially misleading claims

But Murry considers the claims of pluripotency and the ability to develop into any tissue potentially misleading, because they do not give parents the whole picture. He says that transforming stem cells into iPSCs requires highly trained stem cell scientists to reprogramme the cell. “The biobanks store the starting material in a 1000 step journey,” he says, “They don’t provide you with a route to a scientist in a lab.”

“Also, you can make iPSCs from your blood or from your skin as an adult,” Murry adds, meaning that cord blood banking is unnecessary for this process.

Many other private biobanks make similar claims about the therapeutic potential of cord blood. SmartCells, a competing cord blood bank, claims on its website: “As the body’s building blocks, the possibilities for using stem cells are endless. These potent cells are unique because they have the ability to repair, replace, and regenerate cells of almost any kind.”

Future Health Biobank, another private cord blood bank service, lists “treatment possibilities” on its website, naming over 75 genetic, immune, and blood disorders that can be treated with HSCs.

Pietro Merli is a paediatrician at the Bambino Gesù paediatric hospital in Rome, Italy, where he uses HSCs and other cell products to treat his patients. He also believes that the lists of diseases and disorders claimed by the biobanks to be treatable with MSCs and HSCs are unrealistic.

He explains that many of the disorders and diseases he treats with HSCs do not require autologous stem cells, harvested from the patients, and can instead use allogeneic stem cells from donors who are HLA (human leucocyte antigen) matched to patients. “There are many conditions that can be treated with haematopoietic stem cell transplants, but these are allogeneic stem cell transplants, not autologous,” he says.

Merli says that the few instances in which doctors might use autologous HSC transplants are in treating lymphomas. “But you can use your own stem cells from bone marrow, which are harvested during your treatment,” he said, adding that there is no benefit to harvesting and storing stem cells from cord blood.

Merli says that in Italy, where he practises, such advertising by stem cell therapy companies is illegal. He also says that no cord blood bank he has seen details how patients would hypothetically be able to use their preserved stem cells.

Neither SmartCells nor Future Health responded to *The BMJ*’s request for comment.

The Royal College of Obstetricians and Gynaecologists and the Royal College of Midwives do not recommend commercially harvesting umbilical cord blood, unless there’s a specific medical reason to do so.<sup>10</sup>

Murry says the decision whether to bank their infant’s cord blood ultimately lies with parents: “If the cost is not a big deal for you, and it brings you peace of mind, go for it.”

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