

**Lifecell- Daily News Update**

**June 25, 2009**

**Direct Coverage:**

Publication	<a href="http://www.hindu.com">www.hindu.com</a>
Headline	<a href="#"><u>Different diseases pose different challenges</u></a>
Gist of the article	<p>Though he had studied only till eighth standard and works as a carpenter in a private company in Coimbatore, he can rattle out the details of the disease, names of drugs and the various processes involved prior to and after transplantation. Even a veteran doctor would be stunned by his knowledge.</p> <p>Mr. Kumar came to know about his daughter's condition when she was one-and-half-years old. And the struggle began. But fortunately there were many kind souls who helped and guided him at different stages. Friends, doctors, well wishers, anonymous donors, well, the list seems endless.</p> <p>If Dr. Raj took care of transplantation, the Chennai based LifeCell International, a private cord blood bank, helped him in equal measure. "We waived the fee for processing and storing one-year-old Pugazhendhi's cord blood sample," said Mayur Abhaya, Executive Director of LifeCell.</p> <p>The transplantation would have remained a dream but for Pugazhendhi's tissue that perfectly matched Thamirabharuni's. The little brother's blood, which was tested five months after he was conceived, gave the first hope. He was not suffering from the disease. He was only a carrier. Tests done after his birth revealed that the tissue matched perfectly.</p> <p>While he played a crucial role in curing his sister, he could not avoid making her a carrier too. Today, everybody in the family is a carrier.</p> <p>Since it was a perfect tissue match and the donor was her sibling, Thamirabharuni did not face any rejection or graft versus host disease (GVHD) problems.</p> <p>That is not the case with the Surya Mahesh. He was found to be suffering from acute lymphoblastic leukaemia (ALL) stage 3 when he was three years old. He underwent chemotherapy twice. The leukaemia relapsed after the therapy on both occasions.</p> <p><b>Not so lucky</b></p> <p>Surya was not as lucky as Thamirabharuni. There was no relative with a good tissue match. Cord blood had to be procured from the U.S. and Dr. Raj did the transplantation in August last year. The cord blood stem cells, which had only 5/6 tissue match, cured his disease. But he had to battle a severe</p>

	<p>graft versus host disease.</p> <p>“He developed rashes a week after the transplantation. It soon became severe. On the sixth day his skin started peeling,” said his mother. “It peeled off thrice. Soon his nails started falling off and he had severe loose motions.”</p> <p>“We went through a very tough time. It was a big struggle,” she recalled. “But we came out of it.” Biopsy done in April this year tested negative and Surya celebrated his sixth birthday recently.</p>
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Publication	<a href="http://www.hindu.com">www.hindu.com</a>
Headline	<a href="#"><u>Thalassemia cured using cord blood stem cells</u></a>
Gist of the article	<p>Cord blood and bone marrow stem cells with a perfect tissue match from her one-year-old brother were used for transplantation</p> <p>Eight-year-old Thamirabharuni and her one-year-old brother Pugazhendhi share a special kind of bond not commonly seen among siblings. Thanks to her brother, Thamirabharuni no longer suffers from thalassemia disease.</p> <p>The stem cells transplanted in March helped her get rid of thalassemia. And hundred days after the procedure, one can safely say that her disease has been cured.</p> <p>The stem cells that were transplanted came from two different sources — her brother’s cord blood, which was harvested during the time of his birth, and his bone marrow. Stem cells from the bone marrow had to be transplanted as there was insufficient number of stem cells in Pugazhendhi’s cord blood.</p> <p>In the absence of cord blood stem cells, about 200 ml of bone marrow would have been required. It is difficult to get this quantity of bone marrow from a nine-month-old baby.</p> <p>The cord blood was collected by and stored at Chennai based LifeCell International Pvt. Ltd., a private cord blood bank.</p> <p><b>Risk of infection</b></p> <p>So is it all over? “One has to be still careful. There is a risk of infection till the end of the first year [after transplantation],” said Dr. Revathy Raj, Consultant Paediatric Haemato Oncologist, Apollo Speciality Hospital, Chennai. Dr. Raj had done the transplantation for Thamirabharuni and two other cord blood transplantations for thalassemia before this.</p> <p>The fact that patients are on immuno suppressing drugs for one year makes them vulnerable to infections. The risk of rejection of the transplanted stem cells, and the graft versus host disease (GVHD) reduce with time.</p> <p>Thalassemia arises when red blood corpuscles (RBC) production is defective. A person suffers from the disease only when he inherits a defective gene from both parents. He becomes a carrier when he inherits a</p>

defective gene from only one parent. The diseased person has to undergo blood transfusion once every month for the rest of his life.

#### Gold standard

Though stem cells separated from bone marrow have been used for more than 30 years to treat thalassemia, and is a gold standard in treating the disease, cord blood stem cells are slowly becoming an attractive alternative.

Contrary to what is projected by some cord blood banks, doctors are very reluctant to use cord blood stem cells to treat thalassemia in the absence of a full tissue match.

#### Perfect match

“We need a 6/6 [perfect match] for thalassemia. Even a 5/6 match is not sufficient,” asserted Dr. Raj. And doctors refrain from using stem cells from unrelated donors, even if there is a perfect match.

Apart from infections, there are two major challenges from transplantation — graft versus host disease (GVHD) and rejection of the donated stem cells. “There is a 30 per cent chance of having graft versus host disease even when it is from a fully matched related (sibling) donor.” This risk increases to 50 per cent when it is from an unrelated donor, even if there is 6/6 tissue match.

Rejection rate becomes an issue even when there is a perfect tissue match. According to her, in the case of thalassemia, the rejection rate can be up to 20 per cent even with related donors, and up to 40 per cent in the case of unrelated donors.

But why should rejection and GVHD be an issue at all when there is a perfect 6/6 tissue match, and why should it be so high when stem cells are from unrelated donors?

#### Minor HLAs not tested

“There are several minor HLA antigens that are not tested. So if we use stem cells from people belonging to some other ethnic background, there are greater chances of [minor] HLA differences,” Dr. Raj stressed. “And this causes rejection and GVHD.”

In general, greater the tissue match and higher the stem cell count in cord blood, lesser are the chances of rejection and GVHD.

“So why undertake procedures that are risky when thalassemia can be treated through monthly transfusions,” she noted.

Private banking of cord blood for use by the family therefore becomes important when one of the siblings is suffering from a disease that can be cured using it.

#### Case for public banking

Despite the risk of rejection and GVHD, a less than perfect sample can be used to treat children suffering from life threatening diseases such as leukaemia and aplastic anaemia. This is where public cord blood banking

	<p>gains significance.</p> <p>There is a strong case for promoting public banks as depending solely on bone marrow samples will not be wise.</p> <p>Even if a perfectly matched bone marrow donor is found, chances are that the person may no longer be interested in donating.</p> <p>Collecting cord blood samples is easy, the number of samples that can be banked is limited only by resources, and samples can be made available at very short notice.</p>
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**Key Industry News:**

Publication	www.sciencecentric.com
Headline	<a href="#"><u>Stem cell surprise for tissue regeneration</u></a>
Gist of the article	<p>Scientists working at the Carnegie Institution's Department of Embryology, with colleagues, have overturned previous research that identified critical genes for making muscle stem cells. It turns out that the genes that make muscle stem cells in the embryo are surprisingly not needed in adult muscle stem cells to regenerate muscles after injury. The finding challenges the current course of research into muscular dystrophy, muscle injury, and regenerative medicine, which uses stem cells for healing tissues, and it favours using age-matched stem cells for therapy. The study is published in the 25 June advance on-line edition of Nature.</p> <p>Previous studies have shown that two genes Pax3 and Pax7, are essential for making the embryonic and neonatal muscle stem cells in the mouse. Lead researcher Christoph Lepper, a predoctoral fellow in Carnegie's Chen-Ming Fan's lab and a Johns Hopkins student, for the first time looked at these two genes in promoting stem cells at varying stages of muscle growth in live mice after birth.</p> <p>As Christoph explained: 'The paired-box genes, Pax3 and Pax7 are involved in the development of the skeletal muscles. It is well established that both genes are needed to produce muscle stem cells in the embryo. A previous student, Alice Chen, studied how these genes are turned on in embryonic muscle stem cells (also published in Nature). I thought that if they are so important in the embryo, they must be important for adult muscle stem cells. Using genetic tricks, I was able to suppress both genes in the adult muscle stem cells. I was totally surprised to find that the muscle stem cells are normal without them.'</p> <p>The researchers then looked at whether the same was true upon injury, after which the repair process requires muscle stem cells to make new muscles. For this, they injured the leg muscles between the knee and ankle. They were again surprised that these muscle stem cells, without the two key</p>

	<p>embryonic muscle stem cell genes, could generate muscles as well as normal muscle stem cells. They even performed a second round of injury and found that the stem cells were still active.</p> <p>The scientists then wondered when these genes become unnecessary for muscle stem cells to regenerate muscles. It turned out that these embryonic genes are important to muscle stem cell creation up to the first three weeks after birth. What makes the muscle stem cells different after three weeks? The scientist believe that these two embryonic muscle stem cell genes also tell the stem cells to become quiet as the organism matures. After that time is reached, they 'hand over' their jobs to a different set of genes. The researchers suggest that since the adult muscle stem cells are only activated when injury occurs (by trauma or exercise), they use a new set of genes from those used during embryonic development, which proceeds without injury. The scientists are eager to find these adult muscle stem cell genes.</p> <p>'We are just beginning to learn the basics of stem cell biology, and there are many surprises,' remarked Allan Spradling, director of Carnegie's Department of Embryology. 'This work illustrates the importance of carrying out basic research using animal models before rushing into the clinic with half-baked therapies.'</p> <p>The research was funded by the Carnegie Institution, NIH, and the Riley Children's Foundation.</p>
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Publication	www.hindu.com
Headline	<a href="#"><u>In search of stem cells with a perfect tissue match</u></a>
Gist of the article	<p>PIYASHI DUTTA AND SUDESHNA DAS</p> <p>The extensive research on stem cells has revolutionised the way life-threatening diseases like leukaemia and aplastic anaemia can be treated. But there are several steps before these diseases can be treated using stem cells.</p> <p>To begin with, the Human Leukocyte Antigen (HLA)-typing of the patient is done. Doctors then get into the process of finding a matched donor from the computerised list made available to them by National Marrow Donor Programme (NMDP), U.S., and New York Cord Blood Bank.</p> <p>If registration of potential bone marrow donors has been in place for a long time, the emergence of a number of cord blood banks, both public and private, which store the stem cells has gone a long way in helping doctors. Finding a match is just the first step. However, it takes at least three months to procure matched bone-marrow stem cells. It takes just two weeks in the case of cord blood stem cells.</p> <p>The three-month waiting period in the case of bone marrow arises as locating the matched donor very often becomes difficult.</p> <p>It requires a minimum of one to three working days to import the stem cells once the match has been found.</p>

	<p>“We transfuse blood and platelets to aplastic anaemia patients to sustain them till such time matched stem cells are located, procured and transplanted,” said Dr. Revathy Raj, Consultant Paediatric Haemato Oncologist, Apollo Speciality Hospital, Chennai. “In the case of leukaemia, patients undergo a cycle of chemotherapy in the interim period.”</p> <p>An important point worthy of mention is that the bone marrow donor is not required to come to the hospital where the patient is, but rather could go to a nearest hospital in the U.S. to donate his stem cells.</p> <p>In India there are not enough registered bone marrow donors, nor are there proper facilities to harvest bone marrow. Hence the bone marrow cells have to be obtained from organisations like NMDP. The lack of adequate number of donors also results in very slim chances of finding a match in India.</p> <p>India fares better in the case of cord blood banks. India has two public banks – Reliance in Mumbai and Jeevan Stem Cell Bank in Chennai. But even these banks have only a handful of units. This makes the chances of finding a match very remote.</p> <p>Though there are a good number of private cord blood banks in the country, they are of little use to the public. Stem cells banked in these places are made available only to the immediate relative of the donor.</p>
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Publication	www.eurekalert.org
Headline	<a href="#"><u>Human term placenta a new abundant source of hematopoietic cells</u></a>
Gist of the article	<p>Investigators at Children's Hospital Oakland Research Institute, Oakland, California found a way to obtain large numbers of hematopoietic stem cell from human term placenta. The results, which appear in the July 2009 issue of <i>Experimental Biology and Medicine</i>, describe detailed report on quantification, characterization, engraftment capacity, and most importantly, practical way to obtain hematopoietic stem cells from placenta in numbers that are several-fold higher than could be obtained from cord blood.</p> <p>The research team, Dr. Vladimir Serikov, MD, PhD, D.Sci, Assistant Staff Scientist, Catherin Hounshell, a research associate, Sandra Larkin, a research associate, Mr. William Green, student, Dr. Hurokazy Ikeda, MD, Visiting Scientist, Dr. Mark Walters, Medical Director of Children's Hospital Oakland Hematology and Oncology Programs, and Dr. Frans Kuypers, Senior Scientist, performed studies in human term placentas, human cord blood, and immunodeficient mice. Dr. Serikov said, that the fact the human term placenta is a hematopoietic organ was reported by our team for the first time more then a year ago, and this year this finding was confirmed by UCSF scientists headed by Dr. S. Fisher.</p> <p>In this report, said Dr. Serikov, we demonstrate for the first time that human placentas could provide abundant amounts of CD34+ CD133+ colony-forming cells, as well as other primitive hematopoietic progenitors, suitable for transplantation in humans. The total amount of live hematopoietic stem cells, or colony-forming units in culture that could be obtained from</p>

placentas was an order of magnitude larger than the number of hematopoietic stem cells obtained from cord blood from the same source. Hematopoietic stem cells which maintain their differentiation capacity, as well as stromal stem cells that support long-term culture of hematopoietic cells, can be harvested from perfusate of placenta following CXCR4 receptor blockade, said Dr. F. Kuypers. Importantly, live HPCs can similarly be obtained from whole cryopreserved placentas. Cells derived from placental tissue differentiated into all blood lineages in vitro. Animal experiments further demonstrated successful engraftment of placenta-derived HSC, which reconstituted hematopoiesis in immunodeficient mice.

In summary, said Dr. F. Kuypers, our results indicate for the first time that human term placenta is a high capacity source of live and functional hematopoietic stem cells. By using placental circulation and stem cell receptor blockade an abundant amounts of hematopoietic stem cell could be easily obtained in sterile conditions by non-destructive methods.

Dr. Steven R. Goodman, Editor-in-Chief of *Experimental Biology and Medicine* said "the outstanding importance of these results for practical hematology is determined by the fact that total number of stem cells that can be harvested from cord blood limits the efficacy of this stem cell source for transplants only to small children. These novel findings demonstrate that placenta may provide a source of autologous stem cells sufficient for reconstitution of hematopoiesis in adult patients. Use of methods to obtain hematopoietic cells from placenta, developed by Dr. Serikov and Dr. Kuypers as augmentation of cord blood-based therapy or replacement of bone marrow for transplantation will dramatically change whole field of transplantology."