The Made-to-Order Savior

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Points of Access—Pre-Reading

1. Imagine how you would feel if you learned that you had been conceived and born so that someone in your family could be treated for a life-threatening disease. Would it change your feeling of being valued in your family? How? Freewrite for 15 minutes.
2. How might you feel if you learned that one of your siblings had been conceived in order to save your life? Would it change how you thought of your sibling? How?
3. What kind of sacrifice is too great to save one person's life? Is there such a thing? Can you think of a situation where medical technology should *not* be used to save someone's life?

Henry Strongin Goldberg was the first to arrive in Minneapolis. His parents decorated his room on the fourth floor of the Fairview-University Medical Center with his inflatable Batman chair, two Michael Jordan posters, a Fisher-Price basketball hoop and a punching bag hanging from the curtain rod over the bed. They took turns sleeping (or not) in his room for more than a month. It was too risky for his little brother to visit, but there was a playground across the courtyard, and if Henry, who was 4, stood at the window and Jack, who was 3, climbed to the top of the slide, the boys could wave to each other.

Henry had lost his hair by the time 6-year-old Molly Nash moved in down the hall on the bone-marrow transplant unit. Soon she, too, was bald. The two children had always looked alike, just as all children with this type of Fanconi anemia look alike, with their small faces and small eyes and bodies that are tiny for their age. The "Fanconi face" is one more reminder of the claim of the disease. Over time, Fanconi children also come to sound alike, with a deep, mechanical note in their voices, the result of the androgens they take to keep the illness at bay. Once their scalps were bare, Henry and Molly looked nearly identical. But there was one invisible difference between them—a difference that could mean everything.

These two families, the Strongin-Goldbergs and the Nashes, had raced time, death, threats of government intervention and (although they cringe to admit it) each other, to make medical history. The best chance to save a Fanconi child is a bone-marrow transplant from a perfectly matched sibling donor. Many Fanconi parents have conceived second children to save their first, hoping that luck would bring them a match. These two couples became the first in the world not to count on luck. Using in-vitro fertilization, then using even newer technology to pick and choose from the resulting embryos, they each spent years trying to have a baby whose marrow was guaranteed to be an ideal genetic fit.

One family would succeed and one would fail. One child would receive a transplant from a perfectly matched newborn brother and the other from a less well-matched stranger. One would have an excellent chance of survival; the fate of the other was not as clear. Their parents, now friends, would find themselves together in the tiny lounge at the end of the transplant hall, waiting for the new cells to take root, sharing pizza and a pain that only they could understand.

When the rest of the world learned about the baby born to be a donor, there were questions. Is it wrong to breed a child for "spare parts"? ethicists asked. If we can screen an embryo for tissue type, won't we one day screen for eye color or intelligence? There was talk in the news media of "Frankenstein medicine" and threats by Congress to ban embryo research, which had made this technique possible.

It is the kind of talk heard with every scientific breakthrough, from the first heart transplant to the first cloned sheep. We talk like this because we are both exhilarated and terrified by what we can do, and we wonder, with each step, whether we have gone too far. But though society may ask, "How could you?" the only question patients and families ask is, "How could we not?"

Which is why there is virtually no medical technology yet invented that has not been used. It is human nature to do everything to save a life and just as human to agonize over everything we do. The story of Molly and Henry is the story of groundbreaking science. It is also the story of last-ditch gambles on unproven theories, of laboratory technique cobbled from instinct and desperation, of a determined researcher who sacrificed his job and more trying to help and of a frantic drive through a hurricane to deliver cells on time. In other words, it is simply the story of what it now takes, in the 21st century, to save one child.

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Back at the beginning, it was Molly who arrived first. She was born on July 4, 1994, at Rose Medical Center in Denver, and from the start it was clear that something was

terribly wrong. She was missing both thumbs, and her right arm was 30 percent shorter than her left. Her parents, Lisa and Jack, saw her, but could not hold her, before she was whisked off to the ICU, where doctors would eventually find two separate malformations of her heart. (She was also deaf in one ear, but that would not be known until later.) Lisa, wide awake and distraught at 4 a.m. in the maternity ward, made a phone call to the nearby university hospital where she worked as a neonatal ICU nurse caring for babies just like this one, and asked a friend to bring her the book of malformations. Flipping from page to page, she landed on a photo of a Fanconi face and saw in it the face of her newborn daughter.

Named for the Swiss physician who first identified it in 1927, Fanconi anemia causes bone marrow failure, eventually resulting in leukemia and other forms of cancer. Until very recently, children with Molly's form of FA rarely lived past the age of 6, the age Molly is right now. Fanconi is a recessive disorder, which means both parents must pass along one copy of the mutated gene in order for a child to develop the disease. Among the general population, one of every 200 people has a Fanconi mutation. Every ethnic group carries its own genetic baggage, however, and among Ashkenazi Jews like the Nashes and Strongin-Goldbergs, the incidence is 1 in 89, meaning that if both parents are Ashkenazi Jews the chance of having an affected baby is 1 in 32,000. But Lisa, with all her medical training, had never heard of the disease, and Jack, a Denver hotel manager, certainly had not, either.

The holes in Molly's heart closed by themselves, but her other problems remained. She failed to eat, she failed to grow and she was always sick. She had already been through three major surgeries by Oct. 25, 1995, when Henry Strongin Goldberg entered the world at the George Washington University Hospital in Washington. Doctors had warned his parents that he would be quite small, but Laurie Strongin and Allen Goldberg were not worriers, because life had never given them anything to worry about. "Our family history," Laurie says wistfully, "was blue, sunny skies."

Henry was born with an extra thumb on his right hand and a serious heart defect that would require surgery to fix. His parents were devastated, but within days the prognosis worsened. "Fanconi anemia," Laurie wrote in her journal. "If only it was just the heart and thumb. Please take me back a minute ago and make me feel lucky that is it only the heart and the thumb. Fanconi anemia. Rare. Fatal. Henry."

Laurie had spent her career working for nonprofit organizations; Allen had spent his in the computer industry. Both in their early 30's, they were new to parenting and to Fanconi anemia, but they both knew how to navigate a medical database, and within days they found Arleen Auerbach, a researcher at Rockefeller University in New York

and the keeper of the Fanconi patient registry in the United States and Canada, a list that contains about 800 names. Although Molly's parents and Henry's parents still knew nothing of each other, the Nashes had found Auerbach, too, because all Fanconi children eventually find their way to her cluttered Manhattan office.

The rarer the disease, the more it needs a single champion, someone to keep the lists, track the trends, follow the research of others while relentlessly pursuing his or her own. Arleen Auerbach is that person for Fanconi anemia—a sweet, grandmotherly type at the core but with sharp outer edges, armor born of years spent delivering bad news.

She had little but bad news for the Nashes and the Strongin-Goldbergs when they first called. Of the eight separate genes that can mutate and cause Fanconi anemia, Molly and Henry both had Type C, which bares its teeth early and kills often. Had these children been born as recently as 1982, Auerbach explained, there would have been no possible treatment. Bone-marrow transplants—obliterating the faulty immune system and then replacing it with a donated one—used to be fatal for Fanconi patients, because their cells were fragile and crumbled during the chemotherapy and radiation that cleared the way for the actual transplant.

Then, in 1982, doctors in France found that if Fanconi patients were given a significantly lower dose of the chemotherapy drug Cytoxan they could survive. The chances of their survival were increased even further if the donor was a sibling who was a perfect match. The reason for this is found in a web of six proteins that together are known as human leukocyte antigen, or HLA, which is the radar by which bodies recognize what is "self" and what is "intruder." HLA is key to the immune system, and since a bone-marrow transplant is a replacement of the immune system, the HLA of the donor must be as close as possible to that of the recipient, or the new immune system can reject its new container, a life-threatening condition known as graft-versus-host disease.

Over the years it was discovered that the rate of success for sibling transplants was even higher if the sibling was a newborn, because then the transplanted cells could come from "cord blood" taken from the umbilical cord and placenta at birth. These are purer, concentrated, undifferentiated cells, meaning that they are less likely to reject their new body. Back in 1995, when Auerbach first spoke to the Nashes and the Strongin-Goldbergs, the survival odds of a sibling cord-blood transplant were 85 percent, while the odds of a nonrelated bone-marrow transplant were 30 percent and the odds of a nonrelated transplant for patients with Henry and Molly's particular mutation were close to zero.

If there was one thing working in their favor, Auerbach told them, it was that their children's disease was diagnosed so early in life. Fanconi anemia is rare, and few doctors have ever seen a case, which means the condition is often missed or mistaken for

something else. Auerbach has seen too many children with this same Fanconi mutation whose blood fails, with little prior warning, at age 5. Those parents don't have time to do the only thing there is to do, the one thing the Nashes and Strongin-Goldbergs could do—have a baby.

Ten weeks into a pregnancy, Auerbach explained, a chorionic villus sampling test can determine whether the fetus is healthy and if it is a compatible donor. Couples regularly abort when they learn that the unborn child has Fanconi, Auerbach says; having seen the devastation wrought by the disease on one of their children, they refuse to allow it to claim another. Few couples abort, however, when they learn that the baby is healthy but not a donor. "Only three that I know of terminated for that reason," she says. "They were getting older, their child was getting sicker and they were running out of time." Far more common, she says, is for couples to keep having children, as many as time will allow, praying that one will be a match.

Timing a child's transplant means playing a stomach-churning game of chicken with leukemia. The younger a patient is when undergoing a transplant, the better the outcome, because the body is stronger and has suffered fewer infections. On the other hand, the longer the transplant can be delayed, the greater the odds of conceiving a sibling donor, and the better the chance that transplant technology will have improved. The risk of waiting is that every Fanconi patient will develop leukemia, and once that happens a transplant is all but impossible. "You want to wait as long as you can," Auerbach says, "but not so long that it's too late."

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Good doctors learn from their patients, and so it was when Dr. John Wagner answered his telephone one afternoon seven years ago. A lanky, easygoing man, Wagner is scientific director of clinical research in the Marrow Transplant Program at the University of Minnesota, and he says he believes he has performed more bone-marrow transplants on Fanconi children than any other doctor in the country. The caller who set him thinking, however, was not the parent of a Fanconi patient, but rather the father of a toddler with thalassemia, another rare blood disease. The man was calling to inquire about a sibling cord-blood transplant. "You have another child who is a match?" Wagner asked. "No," came the reply. "But we will."

The father went on to explain that he and his wife were using a relatively new technique known as pre-implantation genetic diagnosis, or PGD, to guarantee that their next child would be free of thalassemia. PGD is an outgrowth of in-vitro fertilization; sperm and egg are united in a petri dish, and when the blastocyst (it is still technically

too small to be called an embryo) reaches the eight-cell stage, it is biopsied (meaning one of those cells is removed and screened). Only blastocysts found to be healthy are returned to the womb. Then the waiting game begins—more than two months until it is possible to know if the fetus is a transplant match, then an agonizing choice if it is not. Why, the caller wondered, can't the donor-compatibility tests be done before the embryos are implanted?

Wagner was intrigued by the possibility. Why use PGD just as prevention, he wondered, when it could be used as treatment? Why not, in effect, write a prescription that says "one healthy baby who is going to be a perfect donor"?

Wagner called Mark Hughes, who pioneered the technique and who was working with this family. Hughes is known as a brilliant researcher, simultaneously passionate and wary, a scientist and physician who chose the field of genetics because it combined the intellectual rigor of the lab with the emotional connection to flesh-and-blood patients. In 1994, at about the time he first spoke to Wagner, Hughes was recruited to work at the National Institutes of Health and also as director of Georgetown University's Institute for Molecular and Human Genetics, where his salary was paid in part by the NIH In other words, much of his research was supported by the government. At that time he was also a member of a federal advisory committee that developed guidelines for the type of single-cell embryo analysis that was central to PGD. But no sooner had those guidelines been developed than Congress banned all federal financing of embryo research, and Hughes was forced to continue his research with private funds only.

Under the current Bush administration there is talk of banning all embryo research, even work supported by private funds. For that reason—and for reasons that will become clearer as this tale unfolds—Hughes has developed a healthy distrust of the limelight and refused to be interviewed for this story. As Wagner and Auerbach tell it, Hughes had certainly thought of the possibility of using PGD to determine HLA type long before Wagner called, but he had several concerns.

The ones that weighed heaviest were ethical. It could be argued that using PGD to eliminate embryos with disease helps the patient—in this case, the embryo, the biopsied organism—by insuring that it is not born into a life of thalassemia or cystic fibrosis or Duchenne muscular dystrophy or any of the other agonizing illnesses for which Hughes was screening. Using the same technique to select for a compatible donor, however, does not help the "patient" whose cells are being tested. "It helps the family," says Arleen Auerbach, "and it helps the sibling with Fanconi, but it does not help the embryo."

What Wagner proposed, therefore, would be stepping into new territory. If society gives its blessing to the use of one child to save another, then what would prevent couples

from someday going through with the process but aborting when the pregnancy was far enough along that the cord blood could be retrieved? Or what would prevent couples whose child needed a new kidney from waiting until the fetal kidney was large enough, then terminating the pregnancy and salvaging the organs? What would stop those same couples from waiting until the child was born and subjecting it to surgery to remove one kidney? Once the technology exists, who decides how to use it?

Ethicists think in terms of a slippery slope. But is the potential for abuse in some circumstances reason not to pursue research that can be lifesaving under the right circumstances? Unlike donating a kidney, or even donating bone marrow, donating cord blood involves negligible harm to the newborn donor. The stem cells are collected at birth, directly from the placenta, not from the baby. That is one reason why Wagner argued that HLA testing is ethically defensible. A second reason, he said, was that it is indefensible not to try.

"I'm here as the patient's advocate," he says, meaning Molly and Henry and all the other children in need of transplants. "It's my obligation to push the envelope because I see how bad the other side can be. I see the results of a sibling transplant; they're the easiest transplant to do. And then I walk into the room of the patient who had an unrelated donor, I see that their skin is sloughing off, the mucous membranes are peeling off and they have blood pouring out of their mouths. You cannot imagine anything so horrible in your entire life, and you're thinking, I did this—because there was nothing else available for me to do."

That was apparently what Hughes's gut told him, too, and he agreed to try to develop a lab procedure to screen HLA at the single-cell level. His participation came with certain conditions. First, that the mother must be younger than 35, because younger women produce more eggs, increasing the odds of a healthy match. Second, that he would work only with families who carried a specific subset of the Type C mutation, known as IVS4, because it is the most common. And, last of all, the child being created must be wanted. Only families who had expressed a wish for more children would be approached for this procedure. Hughes did not want to create a baby who was nothing but a donor.

Arleen Auerbach immediately thought of two couples who were the right age, fit the specific genetic profile and who had always planned to have a houseful of children. Her first phone call was to Lisa and Jack Nash in Denver. Without a moment's hesitation, they said yes. Her second call was to Laurie Strongin and Allen Goldberg in Washington.

"If I told you that you could potentially go into a pregnancy knowing that your baby was healthy and a genetic match for Henry, would you be interested?" she asked.

Two hours earlier, Laurie had taken a home pregnancy test. It was positive. If early test results were negative for Fanconi she would carry to term, she answered, even if the baby were not the right HLA type to save Henry's life.

Henry was only 5 months old. His heart surgery had gone smoothly, he was happy and looked deceptively healthy. Fate seemed to be on his side. "If this baby's not a match, we'll try it your way in nine months," Laurie remembers telling Auerbach. "We still thought," she says, "that we had a lot of time."

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Henry became a big brother in December 1995. Jack Strongin-Goldberg was free of Fanconi and was not even a carrier of the disease, so there was no chance that he might pass it on to his own children. His HLA, however, was as unlike Henry's as a biological brother's could possibly be. Laurie and Allen admit that they were briefly disappointed when they heard this last piece of news, three months into the pregnancy. Then they brushed off their psyches and called Mark Hughes, telling him they would be ready to try PGD at the start of the following year.

As baby Jack was being born, Lisa Nash was undergoing the shots and monitoring that are part of in-vitro fertilization. Theirs would be a very difficult case, Hughes had told them. Of the cluster of genes that together determine HLA type, science, at the time, could look at only three. As it happened, Lisa and Jack's patterns were almost identical on those three genes, making it nearly impossible to sort hers from his. That genetic quirk, he warned, could lead to the wrong results. The science to fix this didn't exist yet, he said, and he was figuring it all out as they spoke.

Hughes was also struggling with other problems, ones that had nothing to do with the Nashes' DNA. On the day that Lisa's eggs were retrieved by laparoscopy and fertilized in a dish, the headline in *The Washington Post* read: "NIH Severs Ties With Researcher Who Experimented on Embryos." Hughes had been accused of using federal funds for embryo research, in violation of the Congressional ban. Hughes denied that government money was used for that portion of his work and argued that in any case his research was not even on embryos since all that ever arrived in his lab was DNA extracted from a biopsied cell.

Lisa Nash did not become pregnant.

Mark Hughes resigned from his positions with N.I.H. and Georgetown University rather than agree to stop his research.

The turn of events was devastating for Hughes. He was out of a job and forced to uproot his two young sons and his wife, who was fighting a battle of her own, against

breast cancer. Those close to him say he talked of quitting medicine entirely, so frustrated and angry was he that the rug had been pulled out from under him.

The turn of events was also devastating for the Nashes. "We called him two, three times a week," Jack Nash remembers, and as he speaks a frantic note creeps into his voice. "But he wouldn't return our calls. Months went by, then a year." Over those months they learned that Hughes was moving halfway across the country to a new, privately financed lab where he could continue his work. Then they learned that Hughes's wife was critically ill, that her cancer had spread, that the prognosis was grim. The one thing they did not learn was when and if their quest to save Molly might begin again.

They now understand that science solves the simplest equation first, then moves on to the more difficult ones; their complicated genetic makeup meant their case had to wait. Added to that was the fact that the initial decoding of their DNA had been done at Hughes's former lab in Washington, and he no longer had access to the data. They now also understand that Hughes was in this to save lives, and that having to come to the phone and say that he couldn't, that he didn't know how to match an HLA type for Molly, was more than he could bear. But at the time they didn't understand. At the time they were angry.

"When we manage to speak to him he says we have to give him a few more months to get the lab set up," Jack says. "Meanwhile Molly's counts are dropping and he's the only one who can do this, and he won't help."

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Life for a chronically ill child is a jumble of numbers. The average platelet count in a healthy child: 150,000 to 450,000. The lowest that platelets are allowed to drop before Dr. Wagner urges a transplant: 40,000. Where Henry's platelets hovered when Jack was born: 100,000. The cost of each in-vitro cycle: $11,000. The amount paid by insurance: officially, $0, because the in-vitro fertilization was not being done to treat infertility, nor was it being done to directly treat Henry. The amount the Strongin-Goldbergs raised for Fanconi anemia research at the fundraiser they held on Henry's first birthday: $67,500. The odds of a blastocyst being healthy: 3 in 4. The odds of a blastocyst being a match: 1 in 4. The odds of a blastocyst being a match and also being healthy, and of Laurie becoming pregnant and delivering before Henry had to have a transplant: God only knows.

Since the day Henry's FA was diagnosed, life for Laurie and Allen was filtered through these numbers, through the lens of Fanconi anemia. "Every ensuing pregnancy," she wrote in her journal after baby Jack was born, "will be marred by the fact that the little baby in my belly could have a fatal disease. Every job that Allen and I

consider has to offer medical insurance without excluding pre-existing conditions and with compassion and flexibility. Every relationship has to offer quiet understanding of our travails accompanied by the capacity to give without expecting too much in return."

While Mark Hughes worked to set up his new lab at Wayne State University School of Medicine, near Detroit, the Nashes and the Strongin-Goldbergs were at home, waiting in two very different ways. A crisis can strip a family down to its skeleton of strengths and faults, peeling the niceties away and revealing the bare core of who they are. Henry's parents, for instance, effervescent, embracing and fiercely optimistic from the start, became more so as the clock ran out. They took on Hughes's problems as their own, bonding with him deeply, knowing that they needed him to bond back if they were to save Henry. Molly's parents, in turn, are determined and intense, and they did not waste emotional energy that might be spent protecting their daughter. They were demanding of Hughes, but no more demanding than they were of themselves or of anyone else who could help Molly.

Until the spring of 1997, the two families had still not met. In May of that year, when Hughes was promising both of them that he would be able to resume work soon, a retreat for Fanconi families was held near Portland, Me. The Strongin-Goldbergs went there determined to meet the anonymous couple Arleen Auerbach had mentioned—the couple who had already tried HLA screening with Hughes. Armed with two facts—that the couple had a daughter, and that they lived in Colorado—the Strongin-Goldbergs skimmed the directory and found a family who fit that description.

When Laurie Strongin shook Lisa Nash's hand for the first time she felt an instant bond with the only other mother in the world whose life paralleled her own. Lisa was more reserved. Up to that moment she hadn't realized that the elusive Hughes was working with a second family. Six months later, however, by the time of Laurie's initial in-vitro attempt, the women had paddled past their opening awkwardness and were close telephone friends. When Henry, now 2, talked about his future, he spoke in gradations: first he would be "better," then "super better," then "super-duper better." When all this was over, Lisa and Laurie promised each other, when their children were both "super-duper better," the two families would travel to Disneyworld to celebrate.

In January 1998, when Hughes was finally ready for them, Laurie took the train up to New York City for her appointment with Dr. Zev Rosenwaks, the baby-making guru at the in-vitro fertilization clinic at New York Weill Cornell Medical Center. Henry's platelet count was 71,000 that morning. Eighteen days later, after 18 shots of Lupron, a brutal migraine, hot sweats and cold chills, Laurie's body refused to cooperate, and

the in-vitro fertilization process for that cycle had to be abandoned. That week Henry's platelet count dropped to 31,000, its lowest level up to that point.

Doctors often suggest that in-vitro fertilization patients wait a month or more between attempts, but Laurie didn't have a month, and in early February she was in New York again. This time the numbers were on her side. She produced 24 eggs, and 21 of them were mature enough to be fertilized. Statistically that meant six should be perfect matches for Henry, and three or four of those six should also be disease free.

Sixteen blastocysts survived the biopsy. Allen refused to entrust the cells to anyone, so he flew them to Detroit himself. At the airport he handed his Styrofoam hope chest to a waiting Mark Hughes, then got on the next plane back to New York. The following evening, Laurie was at the Rosenwaks clinic ready for the re-implantation when word came from Hughes. Of the 16 blastocysts tested, 2 were absolutely perfect matches to Henry. Both those matches had Fanconi anemia.

"I'm struggling to come to terms with how much pain I can withstand," Laurie wrote in her journal. She and Allen shared that pain long-distance with the Nashes, who still had not heard when and if Hughes would begin to work with them again. Jack and Lisa were supportive, but also envious and confused. "Were they the family of choice because he liked them better?" Jack remembers wondering. "Is this personal? Does he have something against us, and he's taking that out on Molly? Things like that definitely go through your mind."

The Nashes sent frantic e-mail messages to Hughes, telling him what he already knew—that Molly's counts were dropping and that they were running out of time. In August 1998, when Molly's platelet count had fallen to 30,000, they received his answer. He couldn't help them, he wrote in an e-mail message. Their case was too complicated, both genetically and politically. The genetic analysis he'd so painstakingly done on them belonged to the NIH. "We tried to get the lab at Georgetown to help us, since they were key in our being able to do this for you the first time around," Hughes wrote. The lab has been ordered by the "Catholic administration" of the university "not to get involved 'in any way.'"

Hughes continued: "Go ahead without us. You are anxious, and we understand that very well. But I cannot make this work today and I don't know when I will be able to do so. I am sorry. Science sucks sometimes."

Reeling, Lisa and Jack called Laurie and Allen, who were about to begin their third in-vitro cycle—one that would produce 26 eggs, 24 of which were mature and 21 of which would fertilize. Of those, three would be perfect, healthy matches for Henry. The

Strongin-Goldbergs would not share these details with the Nashes because they had come to understand that other people's good news is sometimes too difficult to hear.

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Taking Mark Hughes's advice, the Nashes did go on without him. They'd decided to jump into a cross-your-fingers pregnancy when they learned, almost by accident, of a private clinic in Chicago that had been quietly doing PGD for nearly 10 years, though never for Fanconi anemia. This news was "like opening a door," say the Nashes, who had not realized that other labs in the country besides Hughes's were providing PGD. If this Chicago lab could test for cystic fibrosis and Tay-Sachs, they wondered, why not Fanconi? And if it had the equipment to screen DNA for disease, why not also screen for HLA?

Lisa and Jack brought Molly along on their trip to the Reproductive Genetics Institute, on the theory that doctors couldn't say no with their adorable but ashen-cheeked child in the room. Her platelets were half what they had been a month earlier. She was weak and tired. They could not have walked into a more receptive office. A year earlier, Charles Strom, then the head of the institute's genetics lab, had heard Mark Hughes speak at a genetics meeting about his attempts to screen DNA for an anonymous couple who were trying to have a child who would be a cord-blood match. "It was like a revelation to me," says Strom, a broad, genial bear of a man now at Quest Diagnostics in California, who could, at that time, perform PGD for 35 diseases but had never thought of HLA screening. "This is what pre-implantation genetics should be about."

A few in the audience expressed their disapproval, he remembers, fearing that this was a step on the road to eugenics. Strom, on the other hand, was enthusiastic. "I stood up and said I thought this was great," he says. "I'm trained not just as a geneticist, but as a pediatrician, and I was tired of watching kids die. I thought this would be the future, and from then on, I was basically waiting for someone to ask me to do it." So when the very same "anonymous" couple arrived and asked, Strom said yes.

He immediately discovered what Hughes had struggled with for years—the "nightmare" caused by the near-identical patterns in the HLA portion of Jack and Lisa's DNA. But he and his team tried something new—they looked farther down the strand, beyond the three known genes, to a spot where it was easier to differentiate one parent from the other. This increased the risk of being wrong, but Molly's blood counts were dropping, and they did not have time to waste. "This isn't what we want to do, but it will probably work," Strom told the Nashes two months after they first met.

It is one thing to screen embryos; it is another to become pregnant, and adding HLA screening to Fanconi anemia screening lowers the odds even more. Only 1 in 6 blastocysts is likely to be both healthy and a matched donor, and that one might not be the quality that the reproductive endocrinologist would have chosen under ideal circumstances. Lisa spent all of 1999 trying to defy those odds. In January she produced 12 eggs, 2 of which were healthy matches; she became pregnant, then miscarried. In June she produced only four eggs, one of which was a match but did not result in a pregnancy. In September she produced eight eggs, six of which had Fanconi anemia; the single healthy match was implanted, but again, her pregnancy test was negative.

In October the Nash family traveled to Minneapolis for Molly's twice-yearly checkup with Dr. Wagner. Her platelets were down to 10,000. In every measurable way she was failing, and she needed a bone-marrow transplant. "You have to stop," Wagner told her parents. It was time to proceed with a transplant from a nonrelated donor. "There comes a point where I have to say: 'It's over. You've done it. You've done the best you could.'"

He began to search for a donor. Lisa and Jack went ahead with the in-vitro that had been scheduled for December. "I couldn't hear the word no," Lisa says. "No' meant Molly could die."

Because they knew it was the last try, and because they needed to feel certain that they had done the best they could, the Nashes insisted on one change of procedure for this final try. It troubled them that Lisa was producing so few eggs per cycle, and they wondered if a different in-vitro fertilization clinic might do better. They approached Dr. William Schoolcraft, an infertility doctor in Colorado known for pushing the envelope. He changed Lisa's hormone regimen and in December 1999 retrieved 24 eggs from her ovaries. For two days the Nashes fantasized about twins and even triplets. Then Strom called to say that there was only one match.

It all came down to one embryo that, statistically, had less than a 30 percent chance of taking hold and staying put. "All it takes is one, all it takes is one," Lisa reminded herself as she drove to Dr. Schoolcraft's office nine days later for a pregnancy test. Minutes after she left, her cell phone rang.

"You're pregnant," said the nurse on the other end.

It was too soon, however, for a happy ending. And indeed, seven weeks into the pregnancy Lisa had just gotten out of the shower when deep red blood began flowing down her legs. The drive to Schoolcraft's office was a blur, but the memory of the picture on the ultrasound screen is vividly clear: a large gap where the placenta had separated from the uterine wall, and the flub-dub pulses of a tiny, living, beating heart.

Lisa went home and went to bed. She was permitted to get up three or four times a day to use the bathroom and once a week for an appointment with Schoolcraft, nothing more. Every time she stood up she began to bleed. Molly, too weak to really play, was on her own manner of bed rest, and mother and daughter spent entire days lying upstairs together.

In March, Molly's blood tests showed signs of pre-leukemia. Wagner sent more data to the national bone-marrow bank, escalating his search for an unrelated donor. In April, Molly's platelets fell to 3,000. She began to need blood transfusions but fought whoever tried to insert the needle; one particularly rocky weekend Strom flew to Denver from a business meeting in Los Angeles, because he was the only one Molly would permit to start the IV. April became May; May turned to June. Along the way, Lisa asked her doctors what could be done should she spontaneously lose the baby. They began to discuss whether stem cells could be harvested from a fetal liver. And all the while, Lisa was still bleeding—clawing her way through the pregnancy, trying to hold onto her baby while holding off her daughter's transplant.

* * *

Back when the Nashes were deciding whether to go ahead with Molly's transplant or try somehow to wait until summer, the Strongin-Goldbergs were making their own impossible choice: whether or not to give up. Their optimism back in August 1998, when they had three healthy embryos, had long since faded. That in-vitro attempt did not result in a pregnancy. Neither did attempt No. 4, in November, when 30 eggs failed to provide a single healthy match.

Attempt No. 5, in February 1999, was almost more than they could bear. Laurie produced 17 eggs and was waiting to be summoned to the clinic when she received another call instead. Allen had taken to scanning the Detroit newspapers online, knowing that Mark Hughes's wife was dying, but not wanting to pester his friend. The morning of Laurie's retrieval, Allen found the news he'd been dreading in the obituary section. Laurie's ovaries were past the point of no return, so Rosenwaks went ahead with the retrieval and fertilization without any idea who would screen the blastocysts. "I couldn't imagine doing this without our friend on the other end and didn't even know if it was possible," Laurie wrote.

But saving Henry had come to mean as much to Hughes as to Laurie and Allen. The researcher had watched his own life nearly destroyed in defense of this work, and he promised he would be there. Fourteen blastocysts survived the biopsy, and on the morning of Feb. 11,1999, just a few days after Hughes's wife's death, Allen loaded his

Styrofoam box with vials and dry ice and boarded the 11:10 a.m. flight to Detroit. He took the container to the lab, where he was moved to tears to find a large picture of his own son hanging on the wall. Underneath it was the question, "Can we help save Henry's life?"

Allen was certain that this attempt would work. There was bittersweet poetry in the timing: death preceding life and preventing death. But when Hughes called the Strongin-Goldbergs in New York, his news was not the stuff of poetry. There was only one match. It did not result in a pregnancy.

Attempt No. 6 took place in June 1999. Twenty-eight eggs, two healthy matches. No pregnancy. Attempt No .7 came in the middle of Hurricane Floyd. Allen drove his Styrofoam box through the eye of the storm—1,200 miles in 26 hours—and delivered the cells, alive, at 2 a.m. Laurie became pregnant, then miscarried.

Their eighth try took place in February 2000. Laurie was in New York, at the clinic, the morning that Allen raced Henry to the hospital with pneumonia so serious doctors warned it could kill him. Laurie agonized over whether to come home (canceling the in-vitro cycle) or stay where she was. If she left, she was certain Henry would die, because he would have lost this chance for a sibling donor. If she stayed, then she was equally certain that Henry would die—of pneumonia, in a Georgetown hospital, without his mother.

She stayed. Henry received two blood transfusions and was pumped full of three intravenous antibiotics. Laurie produced 21 eggs and only one implantable match. "I did not get pregnant," she says, "and I still haven't recovered from the experience."

As the Strongin-Goldbergs dragged themselves from one attempt to the next, the technology of bone-marrow transplants was changing. Specifically, Wagner was testing a new method of removing T-cells from donor blood. T-cells are the ones that recognize the host as foreign, leading to graft-versus-host disease. Simultaneously, Wagner was using fludarabine, an immunosuppressant that appears to encourage the new cells to engraft, or take root. Based on a tiny sample of patients, Wagner's best guess was that these adjustments to the protocol showed promise, apparently increasing the odds of surviving an unrelated bone-marrow transplant from 30 percent to 50 percent in a Fan- coni anemia patient. This was still far lower than the 85 percent odds of a sibling cord- blood transplant, but better than it had been before.

Laurie went through one last, disappointing in-vitro cycle, then she and Allen grabbed those new 50-50 odds. Wagner warned that it was time to stop, and they knew, from looking at Henry, that he was probably right. Henry had had two platelet and two red-cell transfusions in the past two months, and he had been on Anadrol, a steriod to

boost his blood counts, for two and a half years. There comes a point at which a child is too sick for a transplant, and Henry, like Molly, was all but there. In two and a half years of desperate trying, Laurie had 353 injections, produced 198 eggs and had no successful pregnancy. During the same time period, Henry's platelets fell from a high of 103,000 to a low of 10,000.

"We gave it all we had," Laurie wrote when her last pregnancy test was negative and the family was leaving for Minneapolis, for Henry's transplant. "We worked with the world's best doctors. We hoped. We believed. We were brave. We persevered. And despite all that it didn't work. I am left with my belief system intact. I believe in love and science. Nothing more, nothing less."

* * *

A bone-marrow transplant is a medical resurrection. First doctors all but kill a patient; then they bring him back to life. Treacherous and risky, in the end it all comes down to one squishy plastic bag of pale brown liquid which could easily be mistaken for rusty water from a tap. Henry's bag of marrow was collected from an anonymous donor somewhere in the United States on the morning of July 6, 2000, and was flown to the Fairview-University Medical Center, arriving in Room 5 of the bone-marrow transplant floor around dinnertime. A nurse came in with a Polaroid, snapped a few pictures, then added the bag to Henry's leafy IV tree. There was no blaring of trumpets, no rolling of drums. From 8:15 to 8:30 Central Daylight Time, the fluid dripped soundlessly.

Molly Nash's bag was collected with more drama. Lisa's pregnancy had managed to hold. For months Molly's baby brother had been trying to arrive prematurely, and now that he was due, he didn't seem eager to arrive at all. By the evening of Aug. 29, Lisa had been in labor for 52 hours, insisting she be allowed to continue because she knew that more cord blood could be collected during a vaginal birth. Finally, when it looked as if the baby was in distress, he was delivered by C-section. Dr. Strom—his godfather—collected the cord blood. Lisa cradled both the newborn Adam and the warm intravenous bag in her arms.

"God created Adam in his image," Lisa says, explaining how she chose her son's name. "Adam was the first. And from Adam—from his rib, which is full of marrow—God created woman, which is fitting because God used our Adam to give Molly a second chance at life."

When he was 9 days old, Adam flew with his parents and his sister to Minneapolis. Molly settled into the room down from Henry's for the standard four-month stay—a surreal time when it seems as if every child in the world is having a bone-marrow

transplant, because every child that you see is. Molly went through all that Henry had gone through a month before her, and yet everything was different. She had a higher chance of engraftment and a far lower chance of rejection. Her parents were rubbed emotionally raw watching her suffer in order to live. But then they looked at Henry, whose parents feared he was showing early signs of graft-versus- host disease—something Molly would almost certainly never get. They looked beyond Henry, too, at the eight patients who died in the bone-marrow transplant unit during Molly's endless summer.

In the end, Molly's life was saved. That is the Nashes' answer to people who question their right to manipulate nature. Their right springs from the difference between 30 percent and 85 percent; the difference between Molly and Henry. That is also their answer to those who would urge the government to ban all embryo research because it harms unborn children. The research, they say, saves children like Molly.

"We did what we needed to do to keep our daughter from dying," Lisa Nash says. "That is what any parent would do. Isn't this what parents are supposed to do? How can anything be wrong with that?"

Yes, ethicists say, it is exactly what any parent would do, and that is why it is troubling. Parents are being asked to make a choice not only on behalf of their living child, but also on behalf of their unborn child, and that can be an impossible position when the choices get hard. If Molly were closer to death, for instance, would her parents have terminated the pregnancy and used stem cells from Adam's fetal liver to save her?

"We know people will do anything to save their child," says Jeffrey Kahn, an ethicist at the University of Minnesota, where there was much debate about the decisions of the transplant team at the hospital next door. "Now we are learning what 'anything' really means."

Susan M. Wolf, a professor of law and medicine at the University of Minnesota, says she believes that this case is emblematic of the whole of reproductive technology, which she describes as "a multibillion dollar industry based solely on consumer demand." While it might seem logical in each isolated case to let the parents decide, all those single choices add up to a hodgepodge of technology scattered throughout private clinics and laboratories, with no one authorized to say no.

Wagner and Strom agree. They say they do not believe that they, or any other individual doctor, should have the responsibility of sorting through this thicket alone. "As the technology progresses," Strom says, "I see the possibility that someone will come to us and say: 'While you're screening for Tay-Sachs, how about making sure he's not going to have heart disease, too? And while you're at it, why not check for the gene that predisposes him to lupus or makes him immune to HIV?"

"It has the potential to be abused," agrees Wagner. But the response to that potential, he warns, should not be to ban the research or suspend federal financing of the procedure. "It's not going to go away," he says. "We can't put our heads in the sand and say it doesn't exist. I have a stack of requests this high from all over the world, couples asking if they can come use this technology."

Compounding the problems caused by the current ban on federal financing, he says, is the accompanying lack of federal rules. "It's all been forced into the private sector," he says, "where there are no controls. There should be controls. There should be limits. It is up to us, as a society, to decide what they are."

* * *

Since her transplant, Molly Nash has gone back to school. More accurately, school has started to come to her, but her visiting teacher has to wear a mask during lessons. Her ballet teacher comes for in-home classes, too, and Molly twirls and plies and giggles. Her hair is beginning to grow back. Instead of taking 44 pills every day she only takes 10. She is still fed through a stomach tube that her mother hooks up four times a day, and she doesn't have much of an appetite, which is characteristic of Fanconi anemia. The transplant did not cure her of that disease; it merely erased her risk of developing imminent leukemia. She is still likely to suffer Fanconi's other complications, particularly cancers of the mouth and neck. But those will not show themselves for many years, and, her mother says, "maybe they will have a cure by then."

Henry Strongin Goldberg has been ill almost since the day he left the hospital in Minnesota. While Molly's platelet count is 381,000, Henry's is 15,000..He spent months looking yellow and feeling miserable, moaning instead of talking, the result of a near fatal liver infection that is common in transplant patients because of the drugs they are given to suppress their immune system.

In January, for the first time in his tortured life, his parents were struck full force by the thought that he was dying. "All I can think about," Allen said then, "is how much I'll miss him."

Since then, things have gotten even worse. Allen lost his job at an Internet start-up in January, and although he is now working again, the family has burned through its savings. Laurie, who takes home $600 every other week, has spent months sleepwalking through work, hanging on partly out of a need to have one foot tenuously in the real world but also because Henry needed health insurance. Henry's liver slowly improved, but he then began to lose weight at an alarming rate—20 percent of his body weight within weeks—and his skin began to disintegrate, turning red, scaly and raw. Several

painful skin biopsies were inconclusive, suggesting that this was either an allergy to a medication or a sign of graft-versus-host disease.

While Henry was at the clinic having his skin examined, one doctor noticed that he was dragging his left leg when he walked. Two weeks later his left side became so weak that he could not lift himself to a sitting position in bed. He was rushed back to Minneapolis, where a scan showed a mass of unknown origin in his brain. Doctors operated but were unable to determine the cause. Whatever it was, it may have spread to his chest. Just last week, Henry was rushed to the hospital again—his sixth hospitalization in the past 12 weeks—where doctors found lesions in his lungs.

Of the 21 Fanconi patients who have received transplants within the past two years at Fairview under the new drug protocol that gave the Strongin-Goldbergs so much hope, 13 have survived so far. Of those, Henry is in the greatest danger. The first anniversary of his transplant is this coming Friday, a milestone that no longer seems like a victory.

What might have been another red-letter day will come in October, when the Nashes and the Strongin-Goldbergs had planned to meet in Disneyworld. The Strongin-Goldbergs will not be there. After years of technology and intervention, Laurie became pregnant the old-fashioned way, and her baby is due this fall. Tests show him to be a healthy boy who is not an HLA match for Henry.

Points of Engagement—Reading Comprehension

1. Look up the word "ethics" in your dictionary or online. Using your understanding of that definition, explain in your own words the ethical dilemma Belkin outlines in her essay. Who or what is at stake? Refer to two passages in the text to show how you know.
2. According to Belkin, the doctors she interviewed agree that the technology used to create a viable donor for a child with Fanconi anemia could be abused, but that the related research should not be banned. Name two potentials for abuse mentioned in the essay. Do you think the research should be banned? Why or why not?
3. At the end of the essay the two children profiled—Molly and Henry—end up with very different prognoses. Do an online search for both of them to find out what has happened since Belkin's essay was published. What factors were involved in their respective fates? Do those factors suggest how society might approach questions of medical ethics?