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LEGACY

Zuzia's new skin

A U of M discovery lets a young girl with a rare disease do something others take for granted—wear tights

Zuzia's new skin

IN SEARCH OF A CURE FOR THEIR DAUGHTER'S DEVASTATING SKIN DISEASE, A POLISH FAMILY FINDS HOPE IN A NOVEL TREATMENT DEVELOPED AT THE U

BY NICOLE ENDRES

Nine-year-old Zuzia Macheta pretends she is a ballerina, tiptoeing around in a frilly pink skirt and doing something she has longed to do her entire life—showing off her tights.

Born with a devastating skin disease called epidermolysis bullosa (EB), Zuzia was unable to wear tights—something most little girls take for granted—until recently, because her skin would slough off when she tried to remove them.

Described by University of Minnesota pediatric hematologist-oncologist Jakub Tolar as "the worst disease you've never heard of," EB affects about 1 in 20,000 babies in the United States. It is the result of missing a protein in one's genetic makeup that keeps layers of the skin together.

In the many months she spent at U of M Masonic Children's Hospital, 9-year-old Zuzia Macheta enjoyed reading at the nearby Ronald McDonald House. Her favorite subject? Cats.

PHOTOGRAPHY BY DAVID ELLIS

The Macheta family (from left, Sebastian, Zuzia, Sylwia, and Ala) left behind their lives in Poland so Zuzia could be part of a first-in-the-world clinical study at the U of M. Sebastian and Sylwia shaved their heads in unity with Zuzia when chemotherapy made her hair fall out.

EB can vary in severity. And for some children, like Zuzia, even the slightest friction can result in painful blisters and open wounds.

EB also affects the body's mucosal linings, such as those in the mouth and esophagus, making eating extremely painful. In severe cases, the fingers can fuse together because of the body's constant-but-flawed efforts to repair itself.

In addition, people with EB run the perpetual risk of infection and, over time, become predisposed to skin cancer. The most severe forms of the disease can be fatal.

Sylwia Macheta, Zuzia's mother, recalls a day back in their native Poland when Zuzia fell and badly injured her knees. Zuzia cried out, asking why she couldn't run like other kids without suffering.

"That was the moment I told myself I would do everything in my power to help her," Sylwia says through a translator. "And I was able to keep my word."

CHANCE FOR A CURE

Through social media, the Machetas learned about a clinical trial at University of Minnesota Masonic Children's Hospital, under Tolar's direction, that offers a chance for a cure. The U is the only place in the world where a cure-focused EB therapy is available. Other treatments focus on bandaging to prevent infection.

Then they learned that the travel and treatment would cost about $1.5 million. The amount stunned them. Still, the Machetas set a goal of raising the money within two years.

As part of their fundraising campaign, Zuzia's parents allowed her to go on television and tell her story. "And she said, and this is a direct quote," Sylwia recalls, "'There is a doctor in America. He is magical. He has a way to treat kids like me. He can give me new skin.'"

Within 55 days, the family had met their goal.

A COMPLETELY NEW CONCEPT

At the University of Minnesota, basic-science exploration and patient care are interwoven. Typically, health care professionals identify a need in the clinic, then research scientists set to work on solving the problem. In this case, a parent's plea a decade ago to help her children who were suffering from EB prompted Tolar and his colleagues to start looking for a cure. The mother sought out the team because of their expertise in bone marrow transplantation.

What Tolar and his colleagues discovered after about a year and a half of experimentation was revolutionary: bone marrow transplantation, used primarily to treat blood cancers originating in the bone marrow itself, could help people with a disease in a completely different organ—the skin.

"This had never been done before," says Tolar, who directs the U's Stem Cell Institute. "I didn't know it at the time we started this research 10 years ago, but it opened a totally new field in transplantation biology."

This breakthrough builds on a legacy of innovation in blood and marrow transplantation at the University, where the world's first successful bone marrow transplant was performed in 1968.

"It's important not to see this as a one-off," Tolar says. "It's not. It's really a continuation of what this place is about and how deep we go in traditions."

> "I still catch myself repeating the old warnings—be careful, don't run, you can hurt yourself—and she says, 'Mom, my skin is good now.'"
>
> —Sylwia Macheta, Zuzia's mother

LEARNING FROM THE KIDS

The EB treatment is part of an early-phase clinical trial, but it's also considered the standard of care because there are no other cure-focused alternatives.

"The individuals who have EB, they don't have an option," says Tolar, a Distinguished McKnight Professor and holder of the Edmund Wallace Tulloch and Anna Marie Tulloch Chair in Stem Cell Biology, Genetics, and Genomics. "They are like my kids with leukemia: if you don't do something, they die."

And Tolar isn't one to do nothing. About 30 kids have participated in the clinical trial so far, and Tolar and his team have tweaked the protocol four times. "We have learned from every single kid who has been transplanted," he says.

Zuzia Macheta is the first participant in the most recent arm of the treatment study, which involves receiving a bone marrow transplant from a half-matched donor like a sibling or parent—in Zuzia's case, her younger sister, Ala. It also involves three infusions of special "nurturing" stem cells called mesenchymal stromal cells post-transplant. A small quantity of these cells was harvested from Ala's marrow and then grown in culture, ensuring a perfect match to Zuzia's new immune system.

"The plan is that they will rebuild the skin and the mucosal lining much better than the [bone marrow] transplant alone," Tolar says.

The treatment is technologically intricate and expensive. However, a gift from the Richard M. Schulze Family Foundation has made it available to kids like Zuzia.

Tolar says the flexibility philanthropic support provides is crucial to being able to explore new ideas and change protocols based on evidence in real time. And that makes a huge difference, he says. "It's one of the most satisfying things that can happen—that you actually figure out something that nobody else did, you see something under the microscope that nobody has seen before, and then you take that and make the idea into a product and use it in the clinic. It cannot be much better."

A NEW NORMAL

Indeed, life is much better for Zuzia today. Before her transplant, wounds covered her legs from her mid-thighs to her ankles—hence the ban on tights. Today, she'll proudly show her new skin to anyone. Changing her bandages used to take 90 minutes; now it takes 15 minutes to cover the remaining unhealed skin.

Whereas she never fully bathed because contact with the water caused excruciating pain, Zuzia now takes baths and likes trying out new scented soaps.

She also hated the rain because raindrops hitting her fragile skin could cause harm. "Now she likes rain and describes it as being tickled," her mother says.

Before the transplant, Zuzia ate almost nothing by mouth, instead relying on formula fed directly into her stomach through a tube. Now she is being weaned off of the tube and is discovering foods that she didn't know existed. Pizza is her favorite—so far.

Zuzia's younger sister, Ala, donated the healthy bone marrow that's rebuilding Zuzia's skin and mucosal linings.

Perhaps most important, Zuzia and 7-year-old Ala, who went home to Gogolin, Poland, in December, can now tickle, tackle, and hug each other freely.

"Ala was always told to be careful. Now they jump from bed to bed, they run, they horseplay," Sylwia says. "I still catch myself repeating the old warnings—be careful, don't run, you can hurt yourself—and she says, 'Mom, it's after the transplant. My skin is good now.'

"Dr. Tolar, his gift to us was normalcy."

Nicole Endres *is a contributing editor for* Legacy.

PHOTOGRAPHY BY SCOTT STREBLE