“They call me the Miracle Man,” says retired pilot Dale Liesch. “I survived an awful lot of stuff.”

In 2001, suffering from acute myelogenous leukemia, he was told by his physicians there was nothing more they could do for him. But Liesch refused to give up and came to the University of Minnesota to discuss the possibility of transplantation. Daniel Weisdorf, hematologist and medical director of the adult blood and marrow transplant program, was convinced Liesch would be a good candidate for an innovative transplant procedure, developed in part at the University. In a method that uses less chemotherapy than standard practice, Liesch received blood stem cells collected from his sister and has since made a remarkable recovery.

“I walk three miles a day and train with weights,” adding, “I always think about life, not death.”

Building on Stem Cells

Hematologist and stem cell researcher Dan Kaufman examines transplant patient Dale Liesch, right. Although good sources exist for hematopoietic stem cells, such as bone marrow, peripheral blood, and umbilical cord blood, says Kaufman, “there are limits to all of them, which is why embryonic stem cell work is still of interest.”
Liesch’s treatment is just one in a long line of University breakthroughs that have led to pioneering work in stem cells. A precursor to today’s stem cell research, the world’s first successful bone marrow transplant was performed at the University in 1968. Bone marrow is rich in hematopoietic (“blood-forming”) stem cells, necessary to treat AML and other blood diseases. But beyond bone marrow transplantation, stem cells, the master cells of the human body, offer hope for understanding, treating, and curing many other diseases—work that the University of Minnesota continues to lead.

It was the University’s reputation and innovation in bone marrow transplantation that drew Belgian hematologist Catherine Verfaillie to Minnesota in 1988. Specializing in blood disorders, she came here to study transplantation under physician Philip McGlave, but decided to stay to continue her early research in how healthy and faulty stem cells differ.

What makes stem cells so intriguing is their ability to endlessly reproduce and to differentiate into other types of cells. While adult stem cells typically reproduce the type of cell they have specialized into, embryonic stem cells can differentiate into all cell types that form the human body. Researchers believe stem cells one day may be used to repair damaged tissues due to various conditions such as heart disease, stroke, diabetes, Parkinson’s, or muscular dystrophy.

Verfaillie’s research in adult stem cells was so promising that in 2000 the University established the world’s first multidisciplinary Stem Cell Institute. With Verfaillie as director, more than 500 researchers from various fields collaborate to uncover the mysteries of stem cells. Specialists like neuroscientist Walter Low and cardiology researcher Doris Taylor are exploring how stem cells work in the brain and heart and how they may be used to repair damaged tissue, and clinician John Wagner is using stem cells found in umbilical cord blood to treat rare genetic disorders, Fanconi’s anemia, and sickle cell anemia.

In June, two important developments occurred for stem cell research at the University. The newly opened McGuire Translational Research Facility, devoted to research that bridges the gap between basic science and breakthrough therapies, will provide stem cell researchers the latest in cutting-edge laboratories; and the institute entered an international collaboration with Verfaillie’s alma mater, the Catholic University of Leuven in Belgium. “We will build on the strengths of each University to really push forward stem cell research,” says Verfaillie. This will be accomplished, she adds, by marrying Leuven’s clinical expertise with the institute’s strong background in basic and translational research.

The institute’s most startling basic science discovery occurred in 2002 when Verfaillie found that adult cells derived from bone marrow in mice are able to differentiate much like embryonic stem cells. This capacity occurred in cultures outside the mouse’s body and in vivo (inside the mouse’s body). Verfaillie dubbed these cells multipotent adult progenitor cells, or MAPCs. The study was published in the prestigious journal *Nature*, sparking worldwide interest in the institute’s work.

If adult stem cells can be used to generate various types of cells, perhaps it will be possible to harvest a person’s own stem cells for repair. If cells come from a person’s own body, they would be a perfect match, reducing risk of rejection, a concern in transplantation. Such therapeutic promise is exciting, says Verfaillie, but...
also is premature. Before these cells can be used for treatment, “a large number of studies are still required to fully understand the potential of MAPCs,” she says.

Some people see Verfaillie’s finding as proof that embryonic stem cell research is not needed. She disagrees. “It’s far too early in stem cell research to disregard one type over another,” she says. “Side-by-side comparison of adult and embryonic stem cells must be done to determine which stem cells, adult or embryonic, are most useful in treating a particular disease.”

Part of that discovery comes from basic science research—understanding the biology of how stem cells work, before any clinical testing or application occurs. Hematologist Dan Kaufman, using federally approved embryonic stem cell lines, is doing just that. He’s investigating how embryonic stem cells can be specifically directed to make more blood cells. “Once we better understand how to accomplish this,” he says, “we can move on to the clinical translation aspect of our research,” testing on mice, for instance. Clinically, Kaufman sees stem cells as boosting the nation’s blood supply for transfusions. “I don’t think we’re going to replace the Red Cross,” he says, “but it might conceivably provide a supplement.”

Kaufman is also working to identify the genes and proteins that regulate stem cell development, an important aspect of basic science stem cell research, he says. “If we understand the role of genes and proteins, we can apply that to other stem cell research, both embryonic and adult,” making possible the kind of side-by-side comparisons Verfaillie sees as critical to the future of any clinical applications.

Like Verfaillie, Kaufman also was attracted to the University’s strong hematopoietic research and clinical program. “The University’s blood and marrow transplant program is top notch,” he says. As a clinician, “it’s rewarding to be involved with a really innovative program that’s leading the way in a lot of areas, such as umbilical cord blood [another source of stem cells] for transplantation to benefit a greater number of patients.” He adds: “This is the type of institute that allows research to develop into clinical therapies,” which bring new hope to patients like Liesch.

Meri Firpo, recently recruited from the University of California, San Francisco, was drawn to the University’s wide range of expertise and established stem cell researchers. “It’s really valuable to be in a center where other people are looking at other stem cells and asking the same questions, in addition to the clinicians who can instruct us on what they need and what goes wrong to create disease.”

Interested in diabetes, Firpo is investigating embryonic stem cell differentiation in relation to beta cells, which make insulin. She hopes to develop beta cells for transplantation and to understand the normal process of beta cell development. Like Kaufman, she sees the value of using stem cells to understand developmental biology as a means to uncover how disease works. “Even if we haven’t yet used stem cells in therapeutic applications,” she says, “they can be very useful in showing how normal development occurs and how diseases progress.”

She also has experience deriving new embryonic stem cell lines, which she plans to continue at the University using private funds. New cell lines are important for researchers, who require diversity in cells beyond those available prior to President Bush’s cut-off date of Aug. 9, 2001. (Research using ESC lines derived after this date are not eligible for federal funding, but techniques developed since then have been greatly improved, resulting in better quality cell lines.) Firpo expects to first work on lines with mutations...
On June 16, Stem Cell Institute director Catherine Verfaillie and Guy Mannaerts, vice rector for biomedical sciences of the Catholic University of Leuven in Belgium, formally signed an agreement for scientific collaboration on stem cell research between the two universities. Verfaillie, who graduated from Leuven in 1982, will lead the interdisciplinary Stem Cell Center for Excellence in Leuven and continue as director at the University’s Stem Cell Institute for the next few years. Says Verfaillie: “With this multidisciplinary approach of linking basic research directly to the clinical, we will leap forward on stem cell research.” Leuven, surrounded by high-tech companies such as Kodak and Philips, has access to sophisticated imaging capabilities, which are extremely useful in examining how stem cells behave. Meanwhile, the University of Minnesota brings a strong translational research program to the collaboration. Details of the collaboration are still being finalized, but Verfaillie hopes to offer students and faculty endowed funds to travel back and forth to exchange research and ideas.

“Expanding knowledge, globally

For details about stem cell research at the University of Minnesota, see the Stem Cell Institute Web page, www.stemcell.umn.edu.

For health information from the University of Minnesota, see the Health Talk & You Web page, www.healthtalkandyou.com. Use the link to sign up for a monthly notice of the latest from the U.