While many scientists hail stem cell research as medicine’s next great frontier, others see it as morally and ethically problematic. In a bid to retain top scientists and maintain its leading research capabilities, the University of Washington has jumped into the center of this national debate by creating a new stem cell research center. But can it accomplish its first mission to raise $50 million for the cause—and position Seattle as the epicenter of this cutting-edge research? >>>>>>>>>>>>>>>> BY SUSAN NAKAGAWA
THE ROOT OF THE DEBATE: SMALLER THAN THE HEAD OF A PIN, THIS SIX-DAY-OLD BLASTOCYST IS COMPOSED OF 100-150 CELLS. THE OUTER LAYER (TAN) WAS SPLIT OPEN USING MICRO SURGERY, TO EXPOSE THE INNER CELL MASS. THESE CELLS CAN BE GROWN IN CULTURE TO FORM LINES OF EMBRYONIC STEM CELLS.
RANDALL MOON CAME TO MEDICAL SCIENCE IN THE MOST UNLIKELY OF WAYS,
dropping out of three colleges in his first year as an undergraduate and directing most of his energy to motorcycles, rock ’n’ roll and going to the beach. It was admittedly a rocky start for a man who would eventually become a leading scientist in the field of developmental biology, but Moon is nothing if not an iconoclast. He did eventually acquire a Ph.D. from the University of Washington—but he credits his unconventional background with providing him the confidence to challenge orthodoxy and question assumptions.

It’s precisely conditions like Parkinson’s, as well as numerous others such as diabetes, cancer, heart failure, blindness and spinal cord injuries, that researchers at the UW Institute believe will benefit from research involving stem cells. They have reason for their optimism. From stem cells, Institute researchers have begun the first steps toward regenerating heart muscles, the retina and the liver. Cancer stem cells are being studied to develop drug therapies to eliminate them. Moon’s lab is working on identifying drugs that stimulate stem cells. It is a field that scientists acknowledge as the next frontier in medical advancement, resplendent with the promise to ease human suffering.

And yet, beyond the promise of great benefit are concerns, doubts and, in some cases, fierce opposition. The stem cell research controversy boils down to what kind of stem cells are used and how they’re obtained. Adult stem cells, present in every living body, engender little controversy. It’s the stem cells that come from embryos that are
THE TERM “STEM CELLS” became part of the American political lexicon when Senator John Kerry and President Bush addressed the importance of such research in the 2004 presidential debates. While Kerry stated he supported embryonic stem cell research, the president flatly said he “came down on the side of life,” defending his 2001 decision to restrict federal funds used in research on embryonic stem cells. Or at least some of them. Here President Bush seemed to equivocate by allowing federal funds to be used on embryonic cell lines in existence prior to his 2001 directive for scientific research. This resulted in 21 lines (a stem cell line is any group of stem cells that came from the same original blastocyst—the collection of cells that precedes development of an embryo) available for research purposes. Reaffirming his position in 2006, the president vetoed a bill that would have allowed federal funding of research on embryonic stem cells scheduled for destruction in fertility clinics (see “Legal Restrictions,” page 108).

In vitro fertilization clinics are home to hundreds of thousands of excess embryos. When a couple is trying to achieve pregnancy, several embryos are created. The unused embryos—the extras—

THE ABCS OF STEM CELLS

There are many dozens of different kinds of cells in the human body, and they all divide to replace themselves. Stem cells are one kind, and they fall into two categories: embryonic and adult.

Adult stem cells exist in various tissues and organs in the human body. They lie dormant until activated by trauma or injury. Because of this, they have a limited capacity to turn into something else.

Therein lies the difference: Embryonic stem cells have the unique ability to transform into any type of cell in the body. Embryonic stem cells come from a blastocyst—an embryo usually five to eight days old. Composed of approximately 100–150 cells, a blastocyst is smaller than the head of a pin. Within the inner core of the blastocyst reside the highly coveted 40 or so stem cells.

Embryonic stem cells are obtained in one of two ways. In vitro fertilization clinics are home to thousands of excess embryos that were created in fertility treatments. A portion of these stem cells are available for medical research, many are destroyed as medical waste, and in rare cases an embryo might be “adopted” and implanted, resulting in a birth.

The second method for obtaining embryonic stem cells is through a process called “somatic cell nuclear transfer.” In this method, the nucleus of a cell (skin cells, for example) is inserted into an egg from which the nucleus has been removed.

Both methods result in creating the stem cell mass which, when removed, proliferates and creates new stem cell lines. A “stem cell line” is any group of stem cells that came from the same original blastocyst. S.W.
are frozen on petri dishes in a state of suspended medical animation. Smaller than the head of a pin, they are composed of approximately 100–150 cells each and bear no hint of a nervous system. Slated for eventual destruction as medical waste, should these embryos be available for medical research? Or are they human life and, as such, entitled to protection? To fuel the intensity of the debate, stem cells obtained through a process called “somatic cell nuclear transfer” (SCNT) raise the issue of human cloning. SCNT results in the creation of an embryo solely from a donated cell that contains DNA identical to the cell donor. Moon notes that this procedure is theoretical and has never been done in the United States. But theoretically, implantation into a uterus (a condition that does not occur in SCNT) could result in a human clone.

In light of President Bush’s restrictions, Moon, Tony Blau and Chuck Murry, all faculty at the UW Medical School, took stock of the situation. Blau and Murry, friends since their medical school days at Duke University, were both involved in research involving stem cells. Murry was attempting to repair damaged heart muscles using stem cells, while Blau was investigating how drugs can control cell proliferation after implantation. It was while promoting a bill before the state Legislature in 2005 that they connected with Moon, thus laying the groundwork for the Institute.

The bill, which would have created an advisory committee to establish guidelines for embryonic stem cell research, failed by one vote. It was a disheartening setback for the three, who, along with patient advocates, had testified repeatedly on behalf of the bill. All three considered relocating to other academic institutions. Things looked bleak, and Blau, a professor of hematology, recalls a somber time. “The presidentially approved stem cell lines were getting old; they were losing their efficacy. We can make the old lines work—to a point. But they’re extremely limited and they break down more easily. Compare the computer you use today to the one you used 10 years ago, and you’ll get the idea.”

Moreover, in 2004, California voters—in a clear rebuttal of President Bush’s prohibition—had passed Proposition 71, which dedicated $3 billion over 10 years to stem cell research. Moon was at a conference on regenerative medicine in San Francisco just after Proposition 71 passed, he says. “The air was tingling. And the keynote speaker said, ‘I hope each and every one of you moves to California—he was serious. And you know, I thought, ‘Right, why not? They’ve got the money, they’ve got the vision and they’ve got the will.”’ Moon falls silent for a moment as if pondering the wisdom of his decision.

But speaking again, as if reminding himself why he’s doing what he’s doing, he adds, “But what they don’t have is this remarkable group of scientists, this existing intellectual and physical infrastructure. I wanted to stay. My colleagues wanted to stay. We got together—Tony, Chuck and I—and looked around. We noted about 75 labs at the UW doing regenerative medicine work! So we proposed this institute to Paul Ramsey, dean of the medical school, and President Emmert. And the University agreed that stem cell medicine was a priority,” says Moon, especially crediting Emmert with saying yes to the Institute. “The issue is whether we can raise the money.”

“You have to remember that stem cell research is our legacy,” says Blau. “The first stem cell transplants were done in 1969 in the old Public Hospital building where Jeff Bezos of Amazon.com now sits. Anyway, doctors took something highly experimental—stem cells—applied them to a deadly procedure—transplantation to fight cancer—and saved lives. Thousands of people owe their lives to stem cells! Drama. Risk. Rewards.” He shakes his head in amazement. “The possibilities are unparalleled.”

Moore, in his miniscule office within the vast medical center complex, says: “We’re playing for keeps. We’ve got to see if we can move things. I’ve got other offers—half the people in this institute can go elsewhere for vastly more money, in better climates. Can we raise the money and do it quickly? Timing is the key now.”

President Bush’s restrictions mean that not one test tube or petri dish obtained with federal funds can be used on embryonic stem cell lines created after 2001. But it’s precisely those post-2001 lines that scientists want so desperately to use—hence the very press of the issue of whether we can raise the money.

LEGAL RESTRICTIONS: It is currently illegal for any federal funds to be used for research that creates or destroys human embryos. But it is legal to conduct privately funded research on stem cells taken from human embryos. In 2001, President Bush, through his executive authority over the National Institutes of Health and the United States Department of Health and Human Services, limited the use of federal funds to only those stem cell lines that were in existence prior to August of 2001. Approximately 21 stem cell lines became available. In July of 2006 President Bush vetoed legislation that would have allowed federal funding of research on stem cells from embryos currently slated for destruction at in vitro clinics, citing the rights of the fetus against medical benefit.

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institutions are as great, greater than that of Boeing and Microsoft. And if we stand by and choose not to be involved? It’s not just that our researchers will go to California and Harvard. The expertise will be developed in other countries. Singapore, France, England."

Smith recognizes that raising money for the Institute is a marathon, not a sprint, but he’s clearly impatient to get things on track. He’s made a lead gift, remarkable in terms of the amount—$5 million—but perhaps more so because there are virtually no strings attached. “The funding is completely, purposefully unrestricted, to be used in whatever way is necessary to support the Institute,” says Smith. A second gift of $1 million from an anonymous donor was also made, to further research on type 1 diabetes. Things have begun.

Med school dean Paul Ramsey recognizes the urgency. “The University of Washington has among the best people in the nation—on the planet, for that matter—doing regenerative medicine with stem cells. The pace of discovery enables new methods to identify the cause of disease and development therapies. Every day. Stem cells are the hope for the future of treating and curing disease, but because of the federal restrictions we’ve got to raise the money privately.”

IF THE UW IS SUCCESSFUL in raising this money, it will have a direct impact on the operation of Dr. Thomas Reh’s lab, which is using the pre-2001 stem cell lines to address blindness. Reh grimaces as he talks about the limitations of the antiquated lines and speaks passionately about the catastrophic effects of blindness, particularly on the young, from conditions such as diabetes. Reh’s lab is at the forefront of using embryonic stem cells to regenerate retinal cells destroyed by disease. Macular degeneration, diabetes and retinitis pigmentosa are leading causes of blindness in the United States. Until recently, once these neural cells were destroyed, nothing offered any hope for restoration of vision. "Corneas regenerate well," notes Reh, "but the retina does not. The cornea is like the lens of the camera, and if scratched, will repair itself through corneal stem cells. But the retina is like the film in a camera—once it’s gone, it can’t be repaired." Or at least that used to be the case.

Reh’s lab recently transformed human embryonic stem cells into retinal cells. Once implanted in the retinas of mice with congenital blindness, the implanted cells appear to connect with the retinal circuits and replace the damaged mouse cells. The team is now assessing and measuring the degree of vision improvement in the mice. “If you had asked me 15 years ago about embryonic stem cells, I would have said, absolutely not. But I’m surprised—and humbled—by biology every day.”

Reh isn’t a physician, but he’s seen firsthand the devastating impacts of blindness on both children and adults. “As researchers we’ve got to push the field forward,” he notes bluntly. “We have the potential to use biology intelligently to understand life in its various stages and to benefit people.”

AS FERVENTLY AS RESEARCHERS are working to advance stem cell therapies, others are fighting to outlaw any research that involves embryos. “It’s not worth it for any reason, for any purpose,” says Dr. Sharon Quick. (continued on page 149)
Kirk’s Story

FOR A MAN WITH A SPINAL CORD INJURY, STEM CELL RESEARCH IS ABOUT HOPE

In 1983 Kirk Hennig was in his mid-20s. The product of an eastern Washington ranching family, Hennig, of Lake Forest Park, was reared on the values of hard work, family, church and flag, a background that evokes the literary landscapes of John Steinbeck or Wallace Stegner. He learned early on about hardship and making do. When a 3-pound bolt hit Hennig’s head during a construction job, 1,000 pounds of force crushed his fifth vertebra, resulting in instant paralysis. When he awoke, he found himself with the newly bestowed label “quadriplegic.”

Hennig talks about the impact of his accident and the price it extracted from him in carefully measured tones. Only when talking about his parents’ anguish and stating that the accident occurred on his mom’s birthday does his voice register a hint of...
the emotional toll it’s taken on his life. Hennig is a religious man; he credits his spiritual faith and his parents’ Christianity with helping him not just survive, but live. “Mine was a sparse upbringing. It’s the kind of background that gives you grit,” he says simply. “Church. Family. Work. You don’t complain, you make do.”

Hennig brings to mind the famous quote, “Character is not made in a crisis—it is only exhibited.”

He says it took him three years to accept that this injury wasn’t a temporary condition. “Here’s the deal,” he says. “I can live with my destiny; I can live with the pain. What I can’t live with is doing nothing, whether for others or simply to make this world a better place. I measure my life by what I do, what I contribute. Am I making a positive difference? Am I contributing?”

When he talks about stem cell research, it’s clear that he’s motivated by much more than his personal situation; he speaks with compassion and urgency about the benefit it might bring to others who suffer catastrophic accidents. But the prospect of even minimal improvement—the ability to move a finger, the ability to regulate some aspect of bowel or bladder function, for example—would add immeasurable benefit to the quality of his life.

Even minimal improvement with spinal cord injuries has long been daunting, but recently Phil Horner’s lab (part of the UW Institute for Stem Cell and Regenerative Medicine) has shown that spinal cord stem cells exist in rodents and continue to regenerate even after injury. Horner notes that until very recently it was believed that after six months no further improvement was possible in spinal cord patients, but that’s been found not to be the case. “Stem cells in the adult spinal cord demonstrate enormous plasticity,” he says. “To date we’ve not been successful in helping people with long-term injury—yet. We need to do more research in this area to find out why this is.

“But we’ve seen that physical activity stimulates stem cells! And this has resulted in increased sensation.” Horner is cautious about drawing conclusions and emphasizes that more research is needed to determine exactly what impact stem cells are having. But, he adds, “When people call for help, I tell them there’s more work to be done—but to not give up.”

Henning is a conservative man who votes more Republican than Democrat, and he speaks with respect of the Office of the President. Yet he is unequivocal about what stem cell research offers people with devastating injuries. “Hope. Stem cell research is about hope. I just flat disagree with the president on this issue. I have no moral, ethical or religious reservations about saving lives. You have to take a stand; you have to move forward; you have to make things happen. At least that’s how I see it.” S.N.

**A 13-YEAR-OLD DIABETIC COULD SEE A CHANGED LIFE IF STEM CELLS CAN BE DEVELOPED INTO INSULIN-PRODUCING CELLS**

Thirteen-year-old Charlie Tarnoff’s self-conscious smile and thin build frame a body just this side of adolescence. His periodic glances toward his mom bespeak the poignancy of this age, where the protection offered by his parents competes with the lure of teenage life. A seventh-grader at Seattle’s Northwest School, he plays on two soccer teams and enjoys watching Ben Stiller movies and hanging out with his friends.

Diagnosed with juvenile diabetes just before he entered kindergarten, he’s a pro at managing the disease. Periodic finger sticks measure his hours, and insulin injections regulate his blood sugar. He doesn’t consider himself different from other children. When asked about the limitations diabetes places on his life, his brow furrows for a moment and he glances at his mother, Suzanne Kotz. “Diabetes doesn’t stop me from doing what I like doing,” he says. His mother’s hesitation is barely perceptible before she nods in agreement. “We’ve told Charlie that we’ll make it possible for him to do what he wants to do,” she says. “And we do.”

But not without a few complications. After Charlie has had a hard day of soccer, one of his parents tiptoes into his room to check his blood sugar while he sleeps. If it’s low, they’ll wake him and give him a glass of juice; if high, a stab of insulin. Diabetes never leaves his parents’ minds. They orchestrate meals, activities, overnight excursions—in short, their lives—around maintaining his blood chemistry. “Juvenile diabetes is an every-two-hour disease,” Suzanne explains. “Blood sugar levels are subject to so many variations—what you eat, when you eat, how you exercise—that failure to pay attention can have devastating consequences,” she says, her voice trailing off.

Those consequences are ever-present. Charlie’s dad, Steve Tarnoff, a physician for Group Health, has seen firsthand the complications that arise with even the most diligent efforts to regulate this disease: blindness, amputation, kidney damage, heart failure. It’s a cruel irony that the longer one has the disease and the better one manages it, the more likely these conditions become.

(continued on page 151)
embryonic stem cell research, according to Burke, is this: Does an embryo possess full human rights from the moment of conception? If the answer is yes, she says, then you have an automatic responsibility to protect that embryo even in cases where the continued gestation is likely to result in the death of the mother. This is a position most people in our society simply do not agree with, she says.

"It's dangerous when we begin to classify who is and who isn't a person," retorts Quick. "History is fraught with such classifications. Slaves were considered two-fifths a person. What about premature babies?" she continues. "Are they less than a person? Anyway, from a scientific point, life begins at conception! Open any biology book and you'll find that to be the case."

Some objections to stem cell research come from an ingrained mistrust of scientific inquiry and institutions. "While scientists profess to be concerned about ethical issues, they really aren't," is how the reasoning goes, and it's simply a matter of time before a grim Orwellian future is played out as fetuses are harvested for body parts and clones are created for organ replacement of "real people."

These arguments work with a sizable minority of people because they are emotional and powerful. They are also, according to Moon, manipulative and false. "Opponents of stem cell research depict images of babies being ripped apart in order to harvest limbs, a deliberately repugnant and untrue depiction," says Moon. "It will be shameful if we don't advance cures to save lives because scientific inquiry is slowed by arguments made on the basis of fear and ignorance."

One local resident who has helped elevate support and bring visibility to stem cell research on the national stage is Ronald Reagan Jr., son of the former president who suffered for many years the devastating effects of Alzheimer's disease. Reagan, a resident of Magnolia since 1994, is now host of the weekday The Ron Reagan Show on 710 KIRO news radio. A passionate advocate for stem cell research, he has no doubt that this research will save lives.

"Most people assume I'm an advocate because of my dad's experience," he says, "and while his condition may have given me some impetus, I've long been fascinated by the incredible scientific promise of stem cells."

Reagan has been vocal and unstinting in his criticism of the current president's limitations on stem cell research, which he attributes to a basic hostility toward science. "At first I was stunned when President Bush put up a roadblock to helping millions of people. But this administration isn't about reality. Creationism is what we're hearing from the leader of the
free world! It’s outrageous.”

Reagan believes it’s inevitable that stem cell research will continue and notes that 70 percent of the American public supports this endeavor.

Assuming the Institute is successful in raising money, it positions the UW and Seattle to assume not just a role in the pantheon of great American research universities, but a leading role, taking its place among the likes of Harvard, Johns Hopkins and Stanford. Its leaders—scientists of national and international acclaim, community leaders including Bill Gates Sr. and former Governor Dan Evans, the dean of the medical school, the president of the University—all express confidence about the inevitability of this role. And the University has the bona fides, as evidenced by its success in securing research grants, its legacy of Nobel laureates—testaments to its incipient greatness. Boeing, Amazon, Microsoft—all have put Seattle on the map, though in different ways. The Institute may be Seattle’s next great thing. 

The Promise of Stem Cells
(continued from page 104)

Currently, regulating his blood sugar via insulin injections is Charlie’s only option. But embryonic stem cell research could change that. Right now scientists are experimenting with a procedure whereby insulin-producing islet cells are harvested from multiple cadavers and transplanted into diabetic patients, thus restoring the body’s ability to regulate insulin production on its own. The results are extremely promising, but not enough cadavers exist to address even a fraction of those suffering from this disease. A key hope is that embryonic stem cells can be developed into insulin-producing cells; scientists at the UW Institute for Stem Cell and Regenerative Medicine believe that this is only a matter of time. If the research is allowed to go forward, in the future these cells could be infused into Charlie and the more than one million Americans suffering from type 1 diabetes.

Like every family tending a child with a chronic disease, the Kotz-Tarnoff family has been through the crucible, and yet it’s not over. Only when she’s away from Charlie does his mother abandon her measured speech. “He’s our child. We would do anything to take this burden for him. What parent wouldn’t? People who would deny him the promise and potential of innovative medical treatment need to walk in his shoes.” S.N.