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Inside the Korean Cloning Lab

An exclusive, behind-the-scenes look at the laboratory that leads the world in the creation of human embryonic stem cells

By ALICE PARK/SEOUL

The room is warm andÂ still and nearlyÂ dark, bathedÂ only in theÂ light that leaks through its glass door. Refrigerator-size incubators, set to body temperature, line one wall. Along another wall, a young woman in a blue jumpsuit, mask and bonnet is peering through a microscope at half a dozen freshly harvested human eggs. With a glass pipette in one hand and a microneedle in the other, she braces one of the eggs against the tip of the pipette and, as if she were making a stitch, plucks at the membrane, creating a tiny opening. Resting the egg against the pipette, she uses the needle to gently squeeze the cell until the nucleus oozes out, like the center of a jelly doughnut.

This is the sixth-floor lab in Building No. 85 at Seoul National University, the center of operations for Woo Suk Hwang, the South Korean scientist who made headlines last week when he announced that his team, using Dolly-the-sheep techniques, had created 11 human stem-cell lines perfectly matched to the DNA of human patients--a giant leap beyond anything any other lab has achieved. The eggs hollowed out in Building No. 85 were fused with skin cells taken from nearly a dozen patients--ages 2 to 56, suffering from a variety of injuries and disorders--and grown with unprecedented efficiency into early embryos lined with stem cells. The development, published online by the journal Science, takes doctors an important step closer to creating custom stem-cell treatments for everything from Alzheimer's disease to severed spinal cords.

Hwang's methods are controversial, however--particularly in the U.S.--and the White House immediately criticized the experiment. The process is called somatic cell nuclear transfer (SCNT), but most people know it colloquially as therapeutic cloning. "I am very concerned about cloning," President Bush said in response to the news. "I worry about a world in which cloning becomes accepted." If Congress manages to pass a bill it is considering that would lift some of the restrictions on stem-cell research in the U.S., the President promised to veto it.

Scientists, for their part, were singing a different tune. "It's a tremendous advance," says Paul Berg, a Nobel laureate from Stanford University and a major backer of California's independent stem-cell initiative. "The Koreans' work is incredibly impressive," says Stephen Minger, director of the stem-cell biology laboratory at King's College, London. "It is fantastic--a major,

major breakthrough."

The crux of that breakthrough is this: each of the newly created stem-cell lines is genetically identical to one of Hwang's patients. That means any new tissue derived from that patient's cell line can be injected into that individual without triggering an immune reaction. If researchers can figure out how to fix the original defect, they may someday be able to generate replacement tissue that is custom designed to treat the patient's condition. Or at least that's the dream. No one knows yet whether those stem cells can be safely used in people.

Many scientists were astonished by how far the South Koreans had come. Only 15 months ago, Hwang's group created a stir as the first--and so far the only--lab to generate human stem cells via SCNT. Back then it had to use 242 eggs before it was able to create a single, viable set of stem cells from a healthy woman. This time it was able to create 11 stem-cell lines using an average 17 eggs each. "The efficiency is exceptionally high--much higher than I would have thought possible," says Doug Melton, a stem-cell researcher at Harvard University and the Howard Hughes Medical Institute in Boston. "It's about what has been achieved in mouse cells after decades of work."

For Berg, Melton and their American colleagues, there is a touch of envy blended with the praise. Stem-cell research in Asia--not just in South Korea but in China, Japan and Singapore as well--is rapidly outdistancing the work being done in the U.S., reflecting, in large part, real differences in government policy. South Korea, for example, recently banned the use of cloning techniques for the creation of babies but fully supports Hwang's work--to the tune of $2 million a year. By contrast, researchers in the U.S. who want to study human embryonic stem cells are restricted to a handful of federally approved stem-cell lines--most of which, they say, are of such poor quality they cannot be used. Or scientists can forgo federal funding and look to state or private financing for their work. "In this country, we've been stumbling to create public policy," says Melton.

But differences in regulatory environments alone don't explain the South Koreans' success, as TIME's visits to Hwang's lab in early May and again last week made clear. The laboratory is a whirlwind of purposeful activity, and nobody is busier or more focused than Hwang, its director.

Hwang was born just after the Korean War and grew up in a poor rural village in Chungcheong province, three hours from Seoul. "It was difficult to survive," he says. His father died when he was 5, and his mother raised six children by helping wealthier neighbors take care of their cows. After school, Hwang would look after the three cows assigned to his family. He decided then that he wanted to study the animals when he grew up.

A veterinary scientist by training, Hwang says his pioneering work with human stem cells would not have been possible without an extensive animal-research program. Building on what he learned from his experiments on cows, pigs and ducks, Hwang developed his own assembly

line of nearly two dozen steps to improve the efficiency of human stem-cell production. "I wanted to develop a unique technique, not just mimic and modify what others had done," he says.

For example, whereas Hwang's assistants gently squeeze the nuclei from eggs donated by female volunteers, researchers at other labs use a microaspirator to suck out the contents, which Hwang believes may damage the eggs unnecessarily. "Professor Hwang jokes that we're good at manipulating the egg this way because we can use chopsticks," says Okjae Koo, one of the graduate students in the lab.

After DNA from a human patient is inserted into a hollowed-out egg, the fused cell is stimulated electrically and chemically to get it to start dividing. At that point, other researchers have used animal-based growth factors and feeder cells to sustain the growing egg, but that creates problems if the cells are going to be used to treat humans. So Hwang has concocted a growth medium made of human-based nutrients, starting with human skin cells from one of the donor subjects.

When the stem cells inside start growing out onto the underlying feeder cells, the researchers don't try to hurry the process. Most scientists working with embryos left over from in-vitro-fertilization treatments will use chemicals at this stage to separate the cells. "I think the less we manipulate the cells the better," Hwang says.

Such respect for the natural order of things might seem unusual in a scientist whose work seems anything but natural. But for Hwang, generating stem cells is more than just a scientific process. It's no accident that there are more people than machines in Hwang's lab. It's part of an effort on his part to keep the entire procedure as human as possible. He even makes sure that at least one of his researchers keeps the cells company all day and most of the night, as a way of nurturing respect for them. "In this kind of work, you need to insert the human spirit," explains Hwang, who always wears a gold Buddha medallion around his neck. "You need the heart and the spirit, the human touch."

Hwang also takes care to avoid off-putting words such as cloning or therapeutic cloning, preferring instead to call his process nuclear transfer. He doesn't want anyone to confuse his work with reproductive cloning, which he deems "unsafe and unethical." He thinks cloning fully grown humans may be biologically impossible, given the many miscarriages and genetic anomalies that have bedeviled attempts to clone animals, and he doesn't like giving people the impression that therapies or treatment will be available anytime soon.

Indeed, the most immediate benefit of Hwang's work, assuming it can be replicated, will be to better understand how diseases develop. "Rather than having to study the patient or freshly dissected tissues from that patient, we can have a cell line of stem cells that can grow virtually forever," says Hans Keirstead, a neurobiologist at the University of California, Irvine.

"I'm very excited about the possibility of being able to have large amounts of material--for instance, from juvenile diabetes patients--to do research on the complex genetic and nongenetic causes of the disease," says Anne McLaren, a developmental biologist at the Wellcome Trust/Cancer Research Campaign Institute in Cambridge, England. "[That's] going to be the future of cloned stem cells rather than therapeutic cloning."

Meanwhile, the question many researchers are asking is: What will the South Koreans do next? Hwang met last week with Scotland's Ian Wilmut, Dolly's cloner, who wants to work with the South Koreans on Lou Gehrig's disease. Similar collaborations are under way at Memorial Sloan-Kettering Cancer Center in New York City and at Johns Hopkins in Baltimore, Md. By the end of last week, however, Hwang was back at his lab in Seoul, putting even more distance between himself and the rest of the scientific world.

--With reporting by Helen Gibson/London and Laura A. Locke/San Francisco

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