

Stemming Controversy

By Blair Beverly

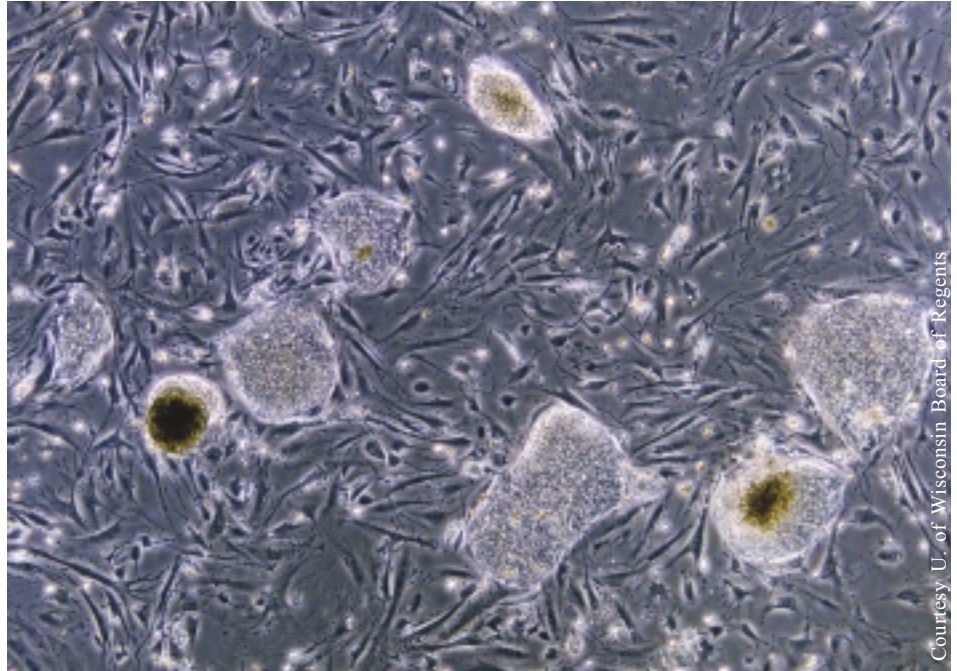
Developing Stanford's Institute for Cancer/Stem Cell Biology and Medicine

“Some Call New Stanford Program Human Cloning,” screamed the December 11 headline from Florida’s *St. Petersburg Times*. Internationally, the reaction was even more critical; “To Clone or Not to Clone?” questioned *The Straight Times of Singapore*, with the subhead “Stanford University plans to clone human embryo, Singapore researchers say move is premature and unnecessary.” Were scientists poised to create a Brave New World here on the Farm? Leading researchers at the recently created Stanford Institute for Cancer/Stem Cell Biology have no such plans, yet headlines from papers across the nation made just such misleading claims after the December 10 announcement of the Institute’s creation. It was a journalistic field day predicated on the sensational story that humans will be cloned at a world-class research university.

In the days after the announcement many more articles were published, displacing the earlier fears of



Dolly (now sadly deceased) was a product of reproductive cloning, not therapeutic cloning like the Stanford Center proposes.



Microscopic 5x view of a colony of undifferentiated human embryonic stem cells being studied in developmental biologist James Thomson’s research lab. The embryonic stem cell colonies are the rounded, dense masses of cells.

people-making with more accurate descriptions of what would really take place at the Institute. Yet these articles only emerged after Institute director Irving Weissman issued a second statement explaining that no reproductive cloning would occur.

Where did the press go wrong, and how did the misleading story spread so quickly? Weissman believes it began with Paul Elias, biotechnology writer for the Associated Press, who after the announcement immediately “shot out his report without checking with us [the Institute], and without mentioning our real objective, which was not cloning human embryos.” The worldwide press picked up Elias’ mistaken wording, promulgating a severe misconception of the Institute’s goals.

Though the press is certainly to blame for not accurately conveying the facts, it is not surprising that the

Institute’s *modus operandi* was misrepresented. There is partly a semantics issue at play, for in the scientific community cloning does not necessarily mean duplicating a human. About five years ago, as human stem cell research was emerging, a distinction emerged between reproductive cloning and nuclear transplantation to produce pluripotent stem cell lines, popularly known as therapeutic cloning. Reproductive cloning involves the creation of an embryo that is then implanted and brought to term, producing a child that is a genetic replica of the DNA donor. Nearly every established scientist has voiced his or her opposition to this form of cloning. Nuclear Transplantation (therapeutic cloning) is far different. Though it starts with the same process of transferring DNA into an enucleated egg to synthesize an embryo, the similarity with reproductive cloning ends

there. The product of nuclear transplantation is allowed to grow for five to seven days in a petri dish, at which point the inner mass of stem cells are removed for tissue culture, and the development halted.

The procedure used to create an embryo is also called somatic cell nuclear transfer (SCNT). Nuclear transplantation, so far only accomplished with mouse cells, begins with unfertilized eggs. The maternal genes in these eggs are removed and replaced by nuclear material from a donated somatic cell. The somatic designation simply means that the cell can come from anywhere in the body except sperm or eggs. An inactive cell similar to the zygote is created by this transfer of nuclear material, but it can be stimulated into development with an electric pulse. Four or five days after its creation, the microscopic ball of a couple hundred cells known as a blastocyst will contain pluripotent stem cells that can develop into

every organ in the body (except the placenta).

The press also failed to mention was that SCNT is a last resort for the Institute. There are other avenues that the Institute will first pursue that do not involve embryonic stem cells. Much of the research will likely employ somatic stem cells, or body cells removed from adult tissues. These stem cells exist latently within many types of human tissue repair or regenerate organs. It may be possible to create pluripotent stem cell lines by fusing an adult somatic cell with an already existing embryonic stem cell line, itself derived from an authentic human blastocyst from an *in vitro* fertilization clinic, one of the 64 cell lines permitted by President Bush. It would be most useful if the somatic cell came from a patient with a genetic disease, so that pluripotent cell lines would be available to study the disease. The Institute may never have to use unfertilized eggs to accomplish the

same ends of enhanced disease understanding.

Still, pluripotent stem cells are of great interest to researchers because they show the most promising capability to develop into all types of cells. The Institute hopes to create a number of pluripotent stem cell lines that carry the genes of a variety of chronic diseases, including Parkinson's, Alzheimer's, and cancer. Having stem cells with inherent genetically mutations that come in patients with diseases of interest will allow researchers to better understand their development and progression. With this enhanced knowledge, more effective treatments may emerge.

One application of the stem cell research is to help patients recover from chemotherapy and immunotherapy. In the normal human body, three processes are at work: cells are "born," they mature, and they die. Usually there are regulations that check how many cells are born, how fast they mature, and



The process by which embryonic stem cells are removed from a fertilized egg.

when they die. In cancer cells, however, this regulatory system has gone awry. Cancer cells reproduce rapidly, mature poorly, and live long—the result is a collection of cells that can invade tissues, possibly disrupting their normal activities.

Before the cancer has metastasized (spread throughout the body via blood vessels), the cancer is localized and treatments can include surgery or irradiation to remove the cancer. However, if it has spread, two techniques are employed. In chemotherapy, drugs are used to target the tissues that contain the cancerous cells; in immunotherapy, the immune system is activated hopefully to attach to cancer cells but not normal cells. The problem is that these treatments can also be very harmful to a patient, so harmful that the patient may be killed in an attempt to kill off the cancer. That is where stem cells can make a critical difference. Chemotherapy and immunotherapy are harmful because in addition to destroying healthy tissue, they also destroy special kinds of stem cells called blood-

forming stem cells, which are responsible for regenerating tissue. A treatment pioneered at Stanford involves transplanting highly purified blood-forming stem cells free of cancer cells and free of the kinds of immune cells that can attack the hosts normal tissues into patients who have had these debilitating cancer treatments, allowing for regeneration of the damaged tissue.

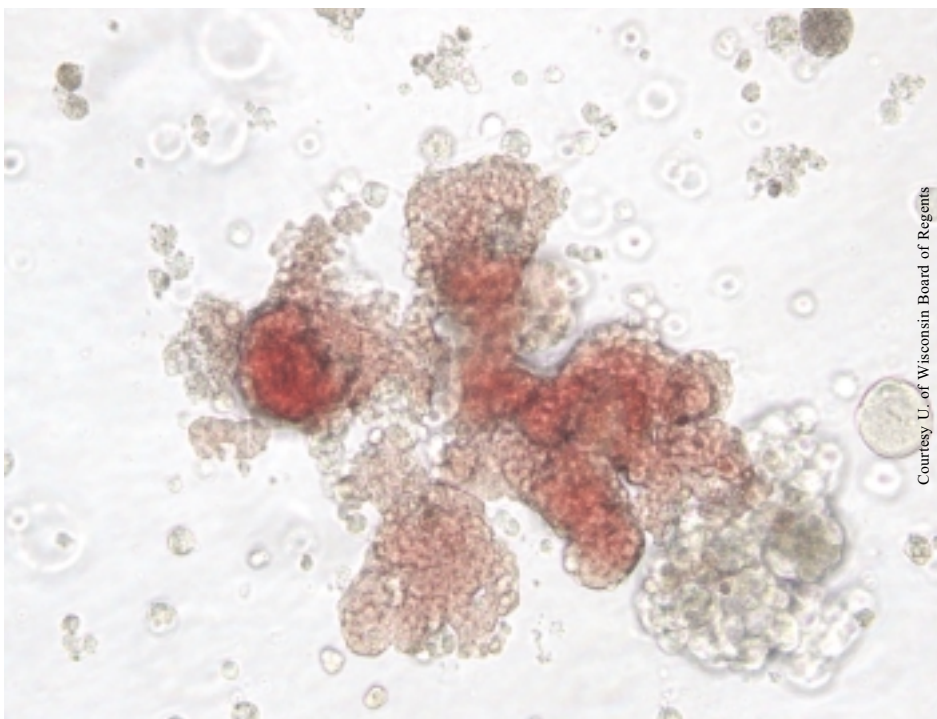
Stem cells can also serve an entirely different purpose in cancer biology. Rather than using research to mitigate the detrimental effects of treatment, stem cell investigation may reveal how the disease emerges and progresses. Cancerous cell populations, like stem cells, are self-renewing. Researchers at Stanford have identified certain genes responsible for this property in stem cells and believe that cancer cells may work in the same way. The Institute wishes to further explore this relationship, with the end goal of developing drug and immune therapies that are specific for cancer stem cells, and that will prevent cancer growth.



Dr. Irv Weissman

Clearly, what will occur at Stanford's Institute for Cancer/Stem Cell Biology and Medicine does not involve cloning human embryos, that is, placing nuclear transplant pseudo-blastocysts into a woman's uterus. There are no plans to work on authentic blastocysts nor to work on nuclear transplant pseudo-blastocysts after that stage of development or after implantation into a uterus. The actual processes employed would never yield a cloned human. But, it is true that the research proposed by the Institute could have a profound and beneficial impact on the lives of millions of people.

Hopefully, the press will portray further scientific research in a more accurate light. Dr. Weissman is not taking any more chances, however. In the future he will work much harder to ensure the press understands the issues by spelling out exactly what is planned and why, including any tricky issues such as nomenclature. Increased caution and communication in the research community seems necessary; public misunderstanding may beget opposition to stem cell research that seeks to cure debilitating disease. It would be tragic if misunderstandings in this politically charged area of research incited public opinion and policymakers to impede the pursuit of revolutionary medical breakthroughs.



Courtesy U. of Wisconsin Board of Regents

Red blood cell colony derived from human embryonic stem cells by scientists at the University of Wisconsin-Madison. The ability to make human blood in the lab may one day augment human blood supplies for purposes of transfusion and transplantation. Toward the same purpose, Dr. Weissman's research has focused on inducing *non-embryo* adult hematopoietic(blood-forming) stem cells to differentiate into new red blood cells.