Caution remains over stem cells despite breakthrough

More technical proof needed before industry commits to controversial research

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News that a South Korean group has for the first time created human embryonic stem cells (ESCs) tailored to individual patients should be increasing pressure on pharmaceutical companies to scale up its involvement in this ethically problematic field. But firms are remaining resistant to the promises of stem cells.

"From a scientific perspective, this is tremendously exciting to the stem-cell community," says John McNeish, Head of Genetic Technologies at Pfizer Global Research and Development. "Yet many advances will be needed to make this more widely accepted in industrial settings," he says.

This is despite the new findings bringing the world of disease-specific stem cells a step closer to reality. The South Korean team, led by stem-cell pioneer Woo Suk Hwang, produced genetically identical human ESC lines from 11 cell-donor patients with rare and common genetic diseases, such as congenital hypogamma-globulinaemia and juvenile diabetes (Hwang, W. S. *et al. Science* **308**, 1777–1783; 2005).

What is also exciting the field is the team's demonstration that their method of creating human ESCs by nuclear transfer is much more efficient than was thought possible. When the same group stunned the world last year by being the first to clone a human blastocyst, only 1 in 200 attempts were successful. In their latest paper the success rate increased by more than tenfold to around 1 in 15.

"This doesn't seem like a big deal, but it's actually huge," says Lawrence Goldstein, Professor of Cellular and Molecular Medicine at the University of California, San Diego. "You are in the realms of getting almost one stem-cell line from one donor."

Jose Cibelli, Professor of Animal Biotechnology at Michigan State University, says this advance is crucial because current egg-donation procedures in women are uncomfortable and carry medical risks. "If such efficiency can be maintained, and even improved, you could now start to think about the possibility of obtaining stem cells from the eggs of patients' relatives," says Cibelli.

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Most of the headlines that greeted the study focused on a new era for regenerative medicine. However, researchers agree that ESCs are still a long way from reaching this goal, although Geron in Menlo Park, California, hopes to begin clinical trials of human ESCs to treat spinal-cord injuries as early as summer 2006.

But a more immediate impact is the exciting prospect of moving disease testing from humans and animal models into the Petri dish. If stem-cell lines are created from people whose conditions are known, drug efficacy and safety, and pharmacogenetic variability could be tested *in vitro*. Disease-specific ESCs could also be differentiated into physiologically and clinically relevant cell types and screened for small-molecule leads.

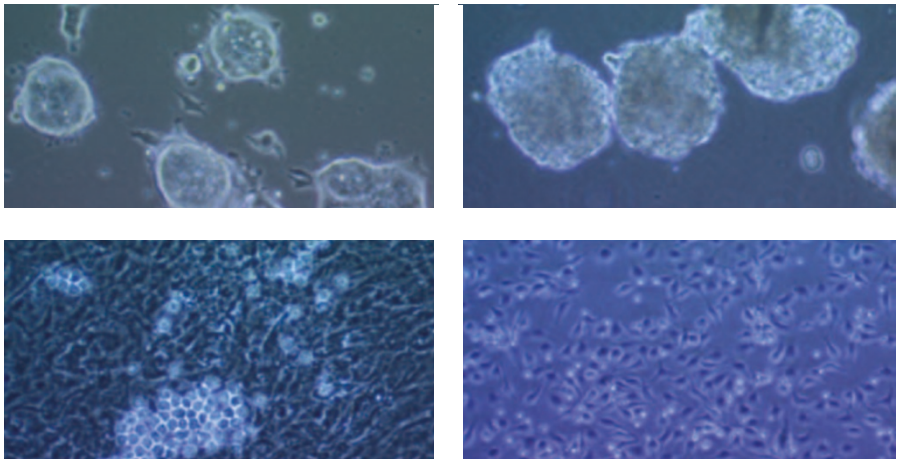
"The [Hwang] study shows that this is technically possible," says Alan Trounson, Scientific Director of Monash Immunology and Stem Cells Laboratories, Monash University, Melbourne, Australia. But he says industry will only become seriously interested once researchers show that the cell lines produced are homogeneous, cellular function is retained during high-throughput screening and that the patient-specific cells truly reflect the disease. "There's a fair bit of work to do to get to this stage," says Trounson. "It's going to take a lot of good, hard scientific slogging before we can show evidence that this can be done."

For instance, cell-differentiation methods need to be fully worked out to aid the generation of the various cells that can be used for biochemistry and cellular experiments. Successes in mouse stem-cell research could help. Stem cells are already being used to generate mouse knockouts, and mouse ESCs are also beginning to be used for high-throughput screening and reproductive toxicology screens.

But there are still several technical limitations with mouse ESCs, says McNeish. "Delivering purified, large-scale volumes of specific, differentiated cells to be used in screening assays is not trivial." And scaling growth of large volumes of human ESC-derived cells will be more challenging, because the doubling time in culture is around three times longer than for the mouse counterparts.

An arguably bigger hurdle is the law, with most countries still banning the creation of disease-specific stem cells. "If you want the field to move quickly, you have to have ten times as many people working on this," says Goldstein. "That's beginning to happen, and papers like this are a shot in the arm for the field."

So, companies will by and large continue to have a healthy degree of scepticism about investing in stem-cell research. Perhaps the biggest indicator of this is the level of correspondence that firms have had with the team behind the latest breakthrough. "I haven't had deep discussions with pharmaceutical companies," says Hwang, Professor of Veterinary Medicine at Seoul National University. "They have only showed initial interest."



Tailored: Researchers have created the first patient-specific embryonic stem cells