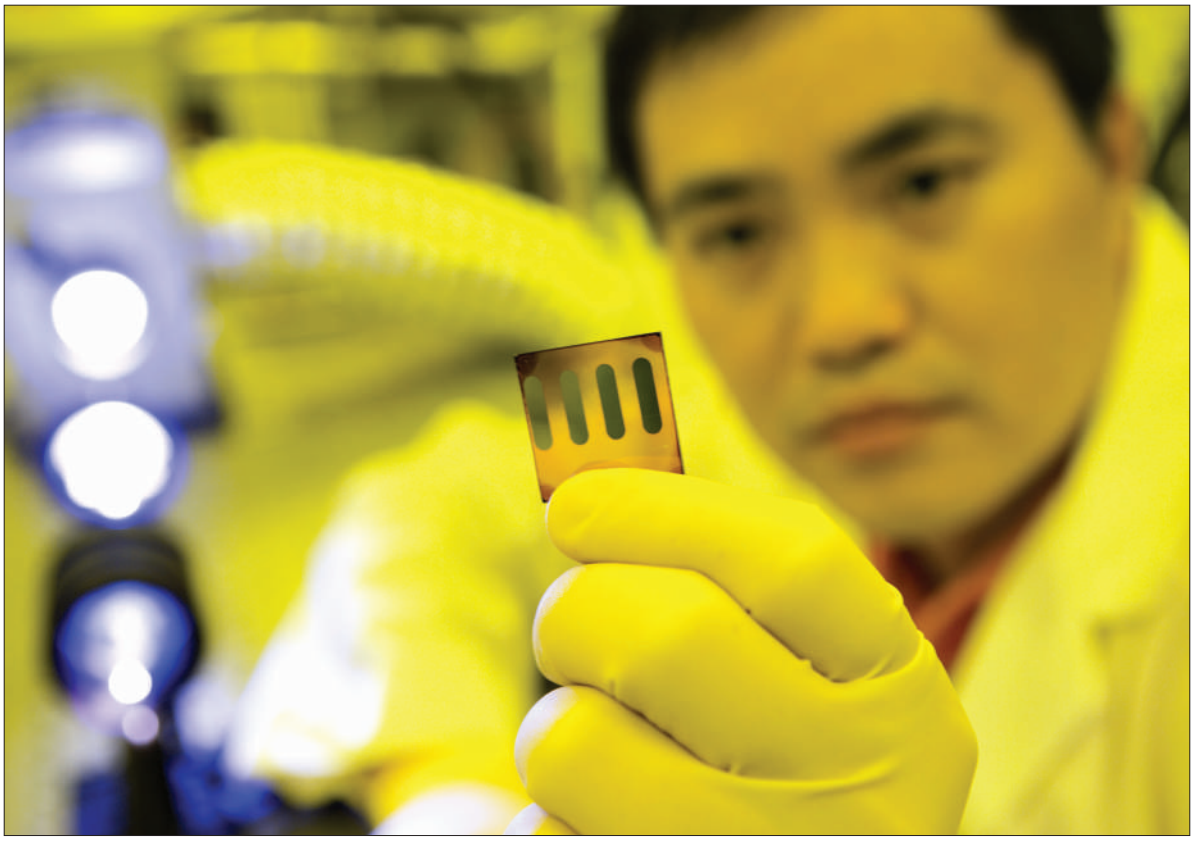

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# Genetic Abnormalities Identified in Pluripotent Stem Cell Lines

***A multinational team of researchers led by stem cell scientists at the University of California, San Diego School of Medicine and Scripps Research Institute has documented specific genetic abnormalities that occur in human embryonic (hESC) and Induced Pluripotent Stem Cell (iPSC) lines.***

Their study will be published in the January 7 issue of the journal Cell Stem Cell.

The published findings highlight the need for frequent genomic monitoring of pluripotent stem cells to assure their stability and clinical safety.

"We found that human pluripotent cells (hESCs and iPSCs) had higher frequencies of genomic aberrations than other cell types," said Louise Laurent, MD, PhD, Assistant professor in the UCSD Department of Reproductive Medicine and first author on the study. "Most strikingly, we observed a higher frequency of genomic duplications in hESCs and deletions in iPSCs, when compared to non-pluripotent samples."

The ability of human pluripotent stem cells to become every cell type in the body has made them potential sources of differentiated cells for cell replacement therapies. "Since genetic aberrations are often associated with cancers, it is vital that cell lines destined for clinical use are free from cancer-associated genomic alterations," said senior author Jeanne F. Loring, PhD, Professor and Director of the Center for Regenerative Medicine at the Scripps Research Institute.

The team identified regions in the genome that had a greater tendency to become abnormal in pluripotent cell lines. With hESCs, the observed abnormalities were most often duplications near pluripotency-associated genes; in iPSC lines, there were duplications involving cell proliferation genes and deletions associated with tumor suppressor genes.

These changes could not have been detected by traditional microscopic techniques such as karyotyping. The team instead used a high-resolution molecular technique called "Single Nucleotide Polymorphism" (SNP) analysis, which allowed them to look for genetic changes at more than a million sites in the human genome.

"We were surprised to see profound genetic changes occurring in some cultures over very short periods of time, such as during the process of reprogramming somatic cells into iPSCs and during differentiation of the cells in culture," Laurent said. "We don't know yet what effects, if any, these genetic abnormalities will have on the outcome of basic research studies or clinical applications, and we need to find out."

Loring concluded: "The results of the study illustrate the need for frequent genomic monitoring of pluripotent stem cell cultures. SNP analysis has not been a part of routine monitoring of hESC and iPSC cultures, but our results suggest that perhaps it should be."

Additional contributors to the paper include Ileana Slavin, Ha Tran, Candace Lynch, Sherman Ku, and Joel Gottesfeld, The Scripps Research Institute; Robert Morey, UC San Diego and The Scripps Research Institute; Franz-Josef Muller, Zentrum für Integrative Psychiatrie, Kiel, Germany and The Scripps Research Institute; Andrew Schork and Carolline M. Nievergelt, UC San Diego; Julie V. Harness and Hans S. Keirstead, UC Irvine; Sunray Lee and Hyun-Sook Park, Modern Cell & Tissue Technologies Inc., Seoul, South Korea; Maria J. Barrero and Juan Carlos Izpisua Belmonte, Salk Institute for Biological Studies and Centro de Medicina Regenerativa de Barcelona; Marina Martynova and Rusian Semechkin, International Stem Cell Corporation, Oceanside, CA; Vasiliy Galat, Northwestern University; Chuck Murry, University of Washington; Ulrich Schmidt, Sydney IVF Stem Cell Laboratory, Sydney, Australia; Andrew Laslett, Commonwealth Scientific and Industrial Research Organisation, Clayton, Australia and Monash University, Victoria, Australia; and Ron Shamir, Tel Aviv University.

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