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Investigators Discover Modified Growth Control in Human Embryonic Stem Cells

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Two papers published by University of Massachusetts Medical School (UMMS) Department of Cell Biology and Cancer Center investigators report striking changes in control of growth in human embryonic stem cells. The studies were carried out on a National Institutes of Health funded grant using two of the six federal government approved human embryonic stem cell lines.

Human embryonic stem cells have the unique capacity of proliferating and becoming specialized during development for formation of tissues and organs. Equally important, some of the human stem cells persist in an unspecialized state and provide a “unique reservoir” of cells for tissue regeneration throughout life, supporting continued renewal of the immune and hematopoietic systems as well as competency for wound healing and “scheduled remodeling” of tissues that include bone, the intestinal lining and skin.

The research team, led by Chair of Cell Biology and Deputy Director of the UMass Memorial Cancer Center Gary S. Stein, PhD, with his colleagues Janet L. Stein, PhD, professor of cell biology, Jane B. Lian, PhD, professor of cell biology and Andre J. Van Wijnen, PhD, associate professor of cell biology, utilized state-of-the-art molecular, cellular and biochemical approaches to establish that the time required for proliferation of human embryonic stem cells is abbreviated (“Self-renewal of human embryonic stem cells is supported by a shortened G1 cell cycle phase,” Journal of Cellular Physiology, Volume 209, Issue 3, Date: December 2006).

Through a systematic probe of the components of the cell division cycle that distinguish embryonic stem cells from more specialized cells, the investigators have identified a reduction in the time between completion of cell division and initiation of DNA replication, the precise duplication of the cell's genes. Particularly significant for understanding biological and clinical relevance, the UMMS team has also defined a specific series of regulatory steps that are bypassed in human embryonic stem cells during cell division ("Establishment of histone gene regulation and cell cycle checkpoint control in human embryonic stem cells," Journal of Cellular Physiology, Advanced Online Publication, November 9, 2006).

The implications of this work are significant. There is a pressing need to enhance capabilities for tissue regeneration, particularly for the treatment of age-related skeletal degenerative diseases that include osteoporosis and osteoarthritis, that can be met by stem cells. Utilizing human embryonic stem cells to reverse the catastrophic complications associated with diabetes, renal failure, multiple sclerosis, muscular dystrophy and Alzheimer's with stem cells is a realistic expectation. And, a stem cell basis for cancer is being widely considered. However, there is much to be learned about the biology of stem cells and a requirement for development of new technologies for stem cell expansion and administration to patients before therapy is a viable option.

Nonetheless, bone marrow-derived stem cell transplantation with "primitive hematopoietic progenitor cells" is a routine treatment for leukemias and non-malignant hematopoietic disorders. The plasticity of human embryonic stem cells offers options where stem cells that are committed to formation of specialized tissues have restricted applications. In the next few years there will unquestionably be advances in scientists' capabilities to propagate human embryonic stem cells and direct them to sites for tissue regeneration and restoration of function to diseased organs.

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