Curr Opin Organ Transplant. 2009 Dec;14(6):694-700.

The effects of low oxygen on self-renewal and differentiation of embryonic stem cells.

Millman JR, Tan JH, Colton CK.

Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, 02139, USA.

PURPOSE OF REVIEW: To summarize recent reports on the effects of low oxygen on the undifferentiated phenotype and differentiation of embryonic stem cells (ESCs). RECENT FINDINGS: The oxygen level to which ESCs are exposed is an important environmental parameter. Under conditions maintaining the undifferentiated phenotype, low oxygen reduces spontaneous differentiation of human ESCs but reduces pluripotency gene expression in mouse ESCs, although reports are conflicting. Differentiation under low oxygen increases generation of neurons, cardiomyocytes, hematopoietic progenitors, endothelial cells, and chondrocytes. Many of the effects of low oxygen have been attributed to action by hypoxia inducible factor-1alpha (HIF-1alpha). The oxygen level in the gas phase (pO2gas) is often different than that experienced by the cells (pO2cell) and is unrecognized by investigators, which makes interpretation of the literature difficult. This difference increases with high cell densities, high cellular oxygen consumption rates, and large medium heights. The problem can be addressed by use of oxygen-permeable culture dishes and by estimation of pO2cell with mathematical models. SUMMARY: Low oxygen influences aspects of ESC pluripotency and differentiation. A better understanding of its effects and mechanism along with better estimation and control of pO2cell is important for applying low oxygen culture to regenerative medicine applications.