

## **Transcriptional signature of human adipose tissue-derived stem cells (hASCs) preconditioned for chondrogenesis in hypoxic conditions.**

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Hypoxia is an important factor involved in the control of stem cells. To obtain a better insight into the phenotypical changes brought about by hypoxic preconditioning prior to chondrogenic differentiation; we have investigated growth, colony-forming and chondrogenic capacity, and global transcriptional responses of six adipose tissue-derived stem cell lines expanded at oxygen concentrations ranging from ambient to 1%. The assessment of cell proliferation and colony-forming potential revealed that the hypoxic conditions corresponding to 1% oxygen played a major role. The chondrogenic inducibility, examined by high-density pellet model, however, did not improve on hypoxic preconditioning. While the microarray analysis revealed a distinctive inter-donor variability, the exposure to 1% hypoxia superseded the biological variability and produced a specific expression profile with 2581 significantly regulated genes and substantial functional enrichment in the pathways of cell proliferation and apoptosis. Additionally, exposure to 1% oxygen resulted in upregulation of factors related to angiogenesis and cell growth. In particular, leptin (LEP), the key regulator of body weight and food intake was found to be highly upregulated. In conclusion, the results of this investigation demonstrate the significance of donor demographics and the importance of further studies into the use of regulated oxygen tension as a tool for preparation of ASCs in order to exploit their full potential.