Mol Cell Neurosci. 2007 Jul;35(3):424-35. Epub 2007 Apr 12.

Oxygen tension controls the expansion of human CNS precursors and the generation of astrocytes and oligodendrocytes.

Pistollato F, Chen HL, Schwartz PH, Basso G, Panchision DM.

Center for Neuroscience Research, Children's Research Institute, Children's National Medical Center, 5th Floor, Suite 5340, 111 Michigan Avenue, N.W., Washington, DC 20010, USA.

Human neural precursor proliferation and potency is limited by senescence and loss of oligodendrocyte potential. We found that in vitro expansion of human postnatal brain CD133(+) nestin(+) precursors is enhanced at 5% oxygen, while raising oxygen tension to 20% depletes precursors and promotes astrocyte differentiation even in the presence of mitogens. Higher cell densities yielded more astrocytes regardless of oxygen tension. This was reversed by noggin at 5%, but not 20%, oxygen due to a novel repressive effect of low oxygen on bone morphogenetic protein (BMP) signaling. When induced to differentiate by mitogen withdrawal, 5% oxygen-expanded precursors generated 17-fold more oligodendrocytes than cells expanded in 20% oxygen. When precursors were expanded at 5% oxygen and then differentiated at 20% oxygen, oligodendrocyte maturation was further enhanced 2.5-fold. These results indicate that dynamic control of oxygen tension regulates different steps in fate and maturation and may be crucial for treating neurodegenerative diseases.