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FUNCTIONAL HUMAN ES-DERIVED OPCs AT LOW OXYGEN

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We have established an efficient system to specify NG2/PDGF-R α /OLIG2+ oligodendrocyte precursor cells (OPCs) from human embryonic stem cells (hESCs) at low, physiological (3%) oxygen levels. This was achieved via both forebrain and spinal cord origins, with up to 98% of cells expressing NG2. Developmental insights reveal a critical role for fibroblast growth factor 2 (FGF-2) in OLIG2 induction via ventral fore-brain pathways. The OPCs mature in vitro to express O4 (46%) and subsequently become galactocerebroside (GALC), O1, and myelin basic protein-positive (MBP+) multibranching oligodendrocytes. These were cultured alongside hESC-derived neurons. The electrophysiological properties of human OPCs are similar to those of rat OPCs, with large voltage-gated sodium currents and the ability to fire action potentials. Exposure to a selective retinoid X receptor agonist increased the proportion of O4+ oligodendrocytes that express MBP from 5% to 30%. Thus, we have established a developmentally engineered system to investigate the biological properties of human OPCs and test the effects of putative remyelinating agents prior to clinical application.