Generation and characterization of spiking and non-spiking oligodendroglial progenitor cells from embryonic stem cells.

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Public Summary:
Pluripotent stem cells (PSCs) have been differentiated into oligodendroglial progenitor cells (OPCs), providing promising cell replacement therapies for many CNS disorders. Studies from rodents have shown that brain OPCs express a variety of ion channels, and that a subset of brain OPCs express voltage-gated sodium channel (NaV), mediating the spiking properties of OPCs. However, it is unclear whether PSC-derived OPCs exhibit electrophysiological properties similar to brain OPCs and the role of NaV in the functional maturation of OPCs is unknown. Here, using a mouse embryonic stem cell (mESC) GFP-Olig2 knockin reporter line, we demonstrated that unlike brain OPCs, all of the GFP+ /Olig2+ mESC-derived OPCs (mESC-OPCs) did not express functional NaV and failed to generate spikes (hence termed "non-spiking mESC-OPCs"), while expressing the delayed rectifier and inactivating potassium currents. By ectopically expressing NaV 1.2 alpha subunit via viral transduction, we successfully generated mESC-OPCs with spiking properties (termed "spiking mESC-OPCs"). After transplantation into the spinal cord and brain of myelin-deficient shiverer mice, the spiking mESC-OPCs demonstrated better capability in differentiating into MBP expressing oligodendrocytes and in myelinating axons in vivo than the non-spiking mESC-OPCs. Thus, by generating spiking and non-spiking mESC-OPCs, this study reveals a novel function of NaV in OPCs in their functional maturation and myelination, and sheds new light on ways to effectively develop PSC-derived OPCs for future clinical applications. Stem Cells 2013.

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