BMP Signaling Induces Astrocytic Differentiation of Clinically-derived Oligodendroglioma Propagating Cells.

Srikanth M, Kim J, Das S, Kessler JA.

Abstract

Oligodendrogliomas are a type of glioma that lack detailed investigation due to an inability to cultivate oligodendroglioma cells that faithfully recapitulate their salient qualities. We have successfully isolated and propagated glioma stem-like cells from multiple clinical oligodendroglioma specimens. These oligodendroglioma propagating cells (OligPCs) are multipotent and form xenografts with oligodendroglioma features. Bone morphogenetic proteins (BMPs) are considered potent inhibitors of oligodendrogliogenesis during development; therefore, the effects of BMP signaling in OligPCs were characterized. BMP pathway components are expressed by OligPCs and canonical signaling via Smad proteins is intact. This signaling potently depletes CD133-positive OligPCs, decreasing proliferation and inducing astrocytic differentiation. Furthermore, analyses revealed that cytoplasmic sequestration of the oligodendrocyte differentiation factors OLIG1/2 by the BMP signaling effectors ID2 and ID4 is a plausible underlying mechanism. These findings elucidate the molecular pathways that underlie the effects of BMP signaling on oligodendroglioma stem-like cells. Implications: Stem-like cells are capable of propagating oligodendrogliomas, and BMP signaling potently diminishes their stemness by inducing astrocytic differentiation, suggesting that BMP activation may be effective as a cancer stem cell-targeted therapy.

PMID: 24269952 [PubMed - as supplied by publisher]