The inhibition of 14-3-3-client protein interactions enhances the differentiation of OPCs by promoting their growth. 14-3-3 binding motifs are required for the inhibition of forkhead transcription factor FOXO4 binding to its target DNA (7). Furthermore, 14-3-3 proteins restrain protein phosphatase 2 activity with phosphorylation sites of protein kinase B, a serine/threonine-specific protein kinase that interacts with FOXO3 (8). FOXO transcription factors are involved in the regulation of cell cycle, cell death, and cell metabolism (9). Moreover, e
dimerization is negatively regulated by 14-3-3s, resulting in decreased cell proliferation (10). These phenomena may regulate the balance between cell proliferation and growth. 14-3-3 protein-mediated pathways may inhibit the proliferation of cells to allocate energy to cell growth.

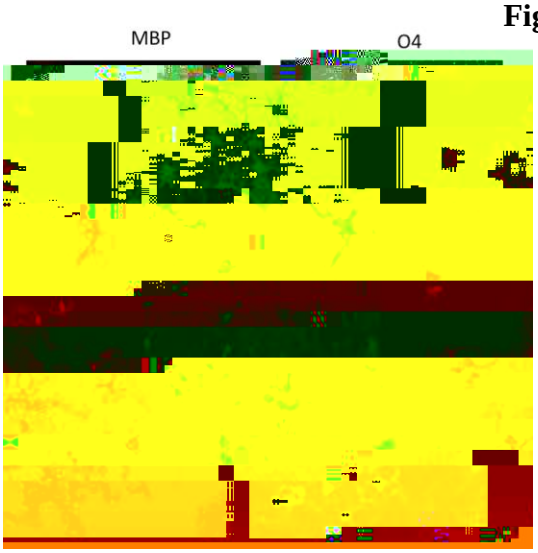
14-3- o stabilize FOXO1, which in turn regulates B cell homeostasis (11). FOXO1 is critical for B cell survival (12). B cells could secrete antibodies against myelin (13). B cells could further exacerbate demyelination by secreting proinflammatory cytokines that induce T cells to attack myelin sheaths (14). This may provide a link between the immune system and the CNS during multiple sclerosis. The inhibition of 14-3-3 activity may lead to enhanced myelination by oligodendrocytes and compromised B cell survival due to destabilized FOXO1.

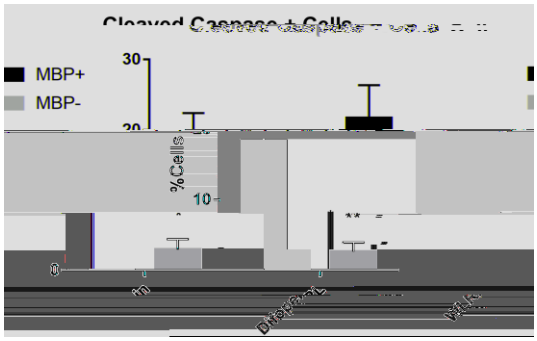
14-3-3s modulate the switch from sonic hedgehog-mediated axon attraction to repulsion during neural development (15). Furthermore, 14-3-3s regulate growth cone turning responses through protein kinase A (16). Both processes involve altering the morphology of growth cones through cytoskeletal rearrangements (17). Therefore, 14-3-3s may mediate pathways that modulate cytoskeletal rearrangements. The observed growth of MBP-positive oligodendrocytes and OPCs due to 14-3-3 activity inhibition may also be regulated by such pathways. Moreover, 14-3-

eye through the RhoA signaling pathway (18). This further demonstrates the implication of 14-3-3s in regulating cytoskeletal structures.

This study showed that inhibition of 14-3-3 protein activity results in increased growth of MBP-positive cells. This is consistent with previous results that demonstrated reduced differentiation of OPCs to oligodendrocytes due to the administration of the 14-3-3-client protein interaction stabilizer, fusicoccin. These findings suggest that inhibition and upregulation of 14-3-3 protein activity may increase and decrease the growth of maturing OPCs, respectively. This research expands the current understanding of the role of 14-3-3 proteins in oligodendrocyte maturation and may pioneer therapeutic strategies to ameliorate demyelination diseases such as multiple sclerosis (19).

Figures





(A) Primary OPCs 2 days in vitro treated with either 1 M BV02 or control (CT) DMSO. **(B)** Area covered normalized to the control group by MBP-positive cells in experimental groups treated with either BV02 or control DMSO. **(C)** Area covered normalized to the control group by MBP-positive cells in experimental groups transduced with either difopein or control WLRL. **(D)** Primary OPCs 2 days in vitro transfected with either difopein or control WLRL plasmid. **(E)** Percentage of cleaved caspase 3-positive cells for difopein experiment for both MBP-positive and MBP-negative cells. **(F)** Expression of different 14-3-3 isoforms in OPCs detected by western blot 2 and 5 days in vitro. Glyceraldehyde 3-

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