TITLE: Regulation of Reactive Astrocyte-Derived Neural Stem/Progenitor Cells by the Sox2 Transcription Factor

ABSTRACT

Stem cells are cells that are multipotential and that have self-renewal capacity. In part, based on these properties, it has been proposed that stem cells have the potential to develop into any cell type and thus may be used to cure numerous diseases**.** Understanding the molecular mechanisms that regulate the activity of stem cells could improve our ability to use them in various medical treatments.

Sox2 is a transcription factor that maintains the multi-potent and self-renewing capacities of neural stem/progenitor cells (NSC) and Embryonic Stem Cells (ES cells). Prior research has shown that inhibition of Sox2 expression in NSCs leads to differentiation and apoptosis. However, in contrast, recent studies showed that Sox2 over-expression in ES cells also induces differentiation and apoptosis. These findings indicate that Sox2 expression levels must be maintained within certain limits in stem cells. However, the effects of Sox2 over-expression in NSCs are not well known.

In a previous study, we isolated Reactive Astrocyte Derived-Neural Stem/Progenitor Cells (Rad-NSCs) from the cortical peri-infarct area 3 days after stroke in mice. We showed that Rad-NSCs possessed multi-potent and self-renewal characteristics *ex vivo*. In this study, using a doxycycline inducible YFP-Sox2 lentiviral vector, we over-expressed YFP-Sox2 in Rad-NSCs. Following doxycycline treatment, Rad-NSCs expressed YFP in culture. Doxycycline treatment decreased Rad-NSC numbers compared with vehicle treatment, suggesting that Sox2 over-expression inhibited cell growth. However, we found that this effect did not occur through reduced proliferation. Rather, apoptosis appeared to play a role in the cell number difference. These findings indicate that Sox2 expression levels must be kept within a narrow range at all times in NSCs.