Title: "Neural activity control of neural stem cells and SVZ niche response to brain injury"

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Date: 11/16/2014

Utilizing stem cells in the adult brain hold great promise for regenerative medicine. Harnessing ability of adult neural stem cells (NSCs) to generate new neurons or other types of brain cells may provide much needed therapies for patients suffering from brain injuries or neuro-degenerative diseases such as Parkinson's, Scizophrenia, or Alzheimer's disease. However, the treatments that involve stem cells are based in NSC transplantation and its efficiency is really low.

The major barriers-to-progress in this area of research are immune-rejection of the implanted cells, faulty tumorogenic growth, but mainly, a faulty integration of the improper progeny. To avoid the problems that accompany NSC transplantation, we wanted to explore whether a new approach focused on "modulating" the brain's own resident stem cells to produce the appropriate cells after brain damage was possible. In order to determine if "in situ" stem cell therapy was plausible, we first had to determine whether 1) Environment provides the right signals for the proper NSC function and generation of the appropriate progeny, 2) whether in vivo NCSs are capable to elaborate an appropriate response under different brain requirements, and 3) whether directed modulation of Neural Stem Cells function is possible.

We found that using genetic alteration in only the neighboring ependymal cells has the profound impact of nearly eliminating new neuron production in the lateral ventricular neurogenic region. Secondly, we determined that cortical strokes that do not impact the neurogenic region induce production on TSP4+ astrocytes that migrate to the injury site to produce the scar that stops cortical bleeding. Thirdly, we have identified a novel cholinergic circuit that resides in the neurogenic region, and that optogenetic stimulation or silencing of acetylcholine neurons can robustly up or down-regulate new neuron production. These three discoveries have met the required conditions for using intrinsic NSCs as therapy for brain regeneration and repair. I am now extending this line of research to determine if this therapy is now a feasible technique for brain repair understanding how the local brain circuits are modified as the NSCs transition to an injury response and back to normal production following recovery. Together these data suggest that therapies utilizing the bodies own intrinsic control mechanisms for NSC regulation may soon provide much needed avenues for future therapies that are unattainable with other methods.