Neural Stem Cell Niche in Acomys

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Abstract

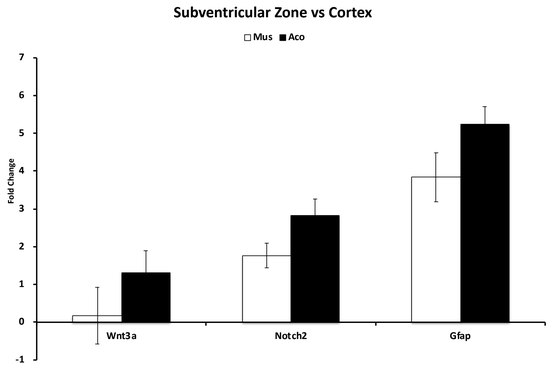
This project investigates the neural stem cell niches and their ability for regeneration in Acomys, a rodent known for regenerative properties. Results revealed that many transcriptions factors and extracellular matrix genes were upregulated in Acomys versus the control, Mus (typical lab mouse).

Introduction

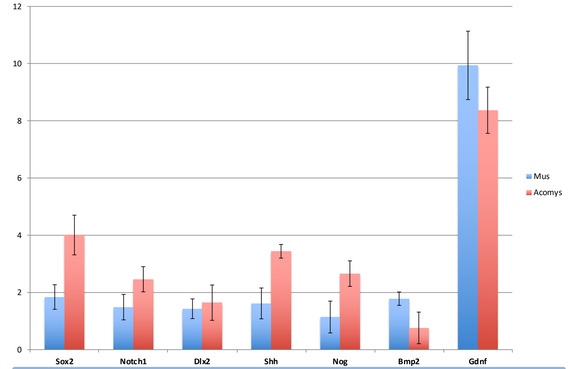
When an adult brain undergoes injury or neurodegeneration it experiences destruction or deterioration of brain cells and in a human, they're not fully regenerated resulting in neuro-dysfunction. There are two areas of the brain that house neural stem cells (NSC), the subventricular zone (SVZ) and the subgranular zone (SGZ) which are neurogenic niches where the brain is responsible for neurogenesis during development, adult life, and regeneration after injury. Mechanisms of the SVZ and SGZ could lead to more treatments and therapies for those with brain diseases or injury. Acomys have greater NSCs than Mus which lead to the hypothesis: How do the unique qualities of the NSC niche in Acomys help maintain more NSCs than Mus? If more NSCs are available to make more neurons, it could have a role in self-renewal after brain injury.

Methods and Results

- RNA extraction: To extract RNA from Acomys and Mus brain samples were used to isolate the subventricular zone followed by a sequence of steps to provide RNA.
- Quantitative Reverse Transcriptase Polymerase Chain Reaction (qRT-PCR): Subventricular zones were dissected from animal brain samples. RNA was extracted and oligo dT primers were used to synthesize cDNA followed by quantitative PCR, to measure the gene expression of the following: Wnt3A, Notch2, GFAP, Sox2, Notch1, Dlx2, Shh, Nog, Bmp2, and GDNF



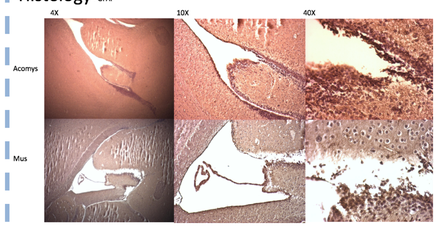
Upregulated in Acomys:
- Wnt3a: Expressed by mature astrocytes that generate neurons
- Notch2: Signaling regulates cell cycle genes to maintain NSC niche.
- GFAP: Marker for B cells.



Upregulated in Acomys:
- Sox2: Positive precursors give to neuroblasts.
- Shh: Maintains adult NSC niche.
- Nog: Regulate the proliferation and differentiation of adult NSCs.
- Notch 1: Signaling governs self-renewal.

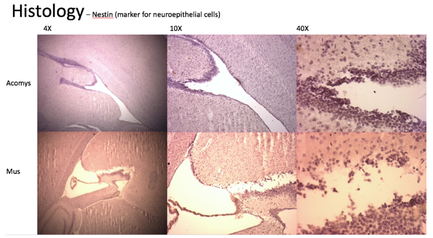
- Antibodies staining results:

Histology - GFAP



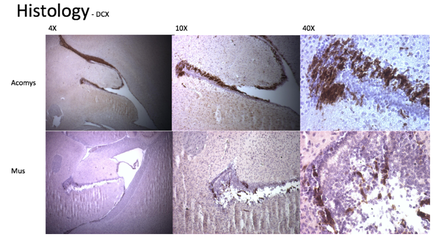
GFAP staining suggested that there was a stringy network of positive cells along the lateral ventricle walls of the SVZ in both species. (primary antibody: anti rat, secondary antibody: biotinylated GFAP)

Histology – Nestin (marker for neuroepithelial cells)



Nestin staining showed few positive cells in both species along the SVZ. (primary antibody: anti rabbit, secondary antibody: biotinylated nestin)

Histology - DCX



The most surprising finding was the DCX stains, which suggested a large amount of positive cells in the Acomys SVZ versus the Mus SVZ. (primary antibody: anti rabbit, secondary antibody: biotinylated nestin)

Discussion

This is an important finding because it speculates that Acomys had more neuroblasts present in the SVZ than in the Mus. In conclusion, the heightened number of upregulated genes in Acomys versus in Mus could help explain why the Acomys' NSC niche can maintain more NSCs. Further research to characterize the NSC niche located in the SVZ should continue. Further understanding on how Acomys NSC niche can maintain more NSC than Mus can lead to more effective brain therapies and treatments that help cure brain injury or degeneration.

References

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