# Cellular Response to Ischemia in Frontal Cortex and Dentate Gyrus

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#### Traumatic Brain Injury & Stroke



#### Neurogenesis After Stroke and Role in Recovery



- Neural Stem Cells (NSCs) → pluripotent
  - Subventricular zone & dentate gyrus
  - Migrate to injured site via rostral migratory stream (RMS)



Bellenchi GC et al. "Adult neural stem cells: an endogenous tool to repair brain injury?" *Journal of Neurochemistry*, vol 14, 2nd edition, 2012, p 159-67.





### Lineage Tracing Mice



- Follows SOX9 progenitors
  - See astrocyte & neural stroke response
  - Novel technique testing
- Sox9 neural stem cells, astrocytes, gliogenesis



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From unpublished paper, edited from:

Mihalas, Anca B. et al. "Intermediate Progenitor Cohorts Differentially Generate Cortical Layers and Require Tbr2 for Timely Acquisition of Neuronal Subtype Identity." *Cell reports* 16.1 (2016): 92–105. *PMC*.

### Objectives of Study

- Characterize frontal cortex & hippocampal response to stroke using a mouse model
- Determine effectiveness of sox9 lineage tracing mice for assessing gliogenic & neurogenic responses to stroke



#### Markers & Roles



- Reelin- glutamatergic cells in radial migration
- Tbr1- transcription factor
- Ctip2- subcortical projecting neurons
- Satb2- callosal projecting neurons
- Cux1- dendritic branching, spine formation
- BRDU- cell birth



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Mihalas, Anca B. et al. "Intermediate Progenitor Cohorts Differentially Generate Cortical Layers and Require Tbr2 for Timely Acquisition of Neuronal Subtype Identity." *Cell reports* 16.1 (2016): 92–105. *PMC*. Web. 9 Aug. 2016.





NEUROLOGICAL SURGERY

#### Stroke Brains Demonstrate Increased Neurogenesis in SVZ after Stroke

Sham Brain



Stroke Brain



BRDU DAPI



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### Sox 9 Lineage Tracing Mice Successfully Labels Progenitors

DAPI SOX9 RFP αSOX9



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#### Sox 9 Lineage Tracing Mice Successfully Labels Progenitors

DAPI

SOX9

![](_page_10_Picture_1.jpeg)

#### Conclusion

- Cortical layer expression reduced across the board after stroke though neurogenesis is greater after stroke (BRDU)
- Sox9 lineage tracing can label newly generated cells in stroke mice;
  - Ependymal cells
  - Choroid plexus
  - Astrocytes
  - NSCs
  - Neurons

![](_page_11_Picture_8.jpeg)

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#### Future Directions

#### ADDITIONAL BRAINS TO CUT $\rightarrow$

	marker	Z18L	B3R	S1	S4	49L	Z15L	11RL	30RR	10L	30R	31L	32RL	A3-2	F-12
cortex	reelin	✓	✓	✓	✓	✓	✓	• TB		nice – c	ut, stair	۱& ima	ge		
	cux1	Х	Х	$\checkmark$	$\checkmark$	Х	$\checkmark$	• Ac	Х	data fo	r Sox9 l	orains			
	SatB2	Х	Х	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	• Ag		;es					
	ctip2	$\checkmark$	Х	$\checkmark$	$\checkmark$	Х	$\checkmark$	• Tre	Х	: investi	gation				
	TBR1	$\checkmark$	Х	$\checkmark$	$\checkmark$	Х	$\checkmark$	•		ulating ı	neuroge	nesis in	to necr	otic core	2
dentate	BRDU			$\checkmark$	$\checkmark$		$\checkmark$	•	Preve	enting n	ecrotic	core/gli	al scarri	ng	
	NeuroD														
	sox2														
	GFAP														
	TBR2														
lineage tracing	GFAP														
	TBR2		Х												
	sox9														
	DCX		Х												
cell	caspase	X	X	X	X	X	X								
death	3														

#### Thank You!

![](_page_13_Picture_1.jpeg)

#### Seattle Children's

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