KING'S College LONDON

INSTITUTE OF PSYCHIATRY,
PSYCHOLOGY & NEUROSCIENCE

Module:
Biological foundations of mental health

Week 2:
Building blocks of the brain

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Topic 2
From embryonic neural progenitor cells to adult hippocampal neurogenesis

Part 3 of 4

Molecular control of Adult Neurogenesis

Molecular control of adult neurogenesis (1)

What we knew back in 2004

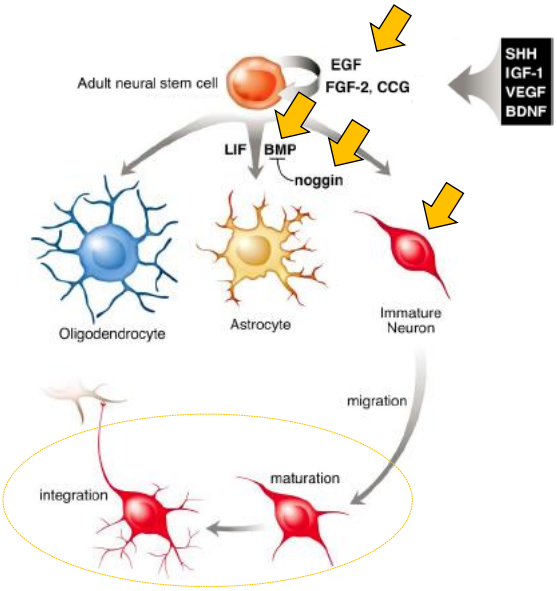

Figure 10: Molecular control of adult neurogenesis

For review, Lie et al., 2004

Molecular control of adult neurogenesis (2)

Proliferation	
miR-124	Decreases proliferation
Shh	Increases proliferation
Sox2	Increases proliferation
Tlx	Increases proliferation
Wnt	Increases proliferation
Differentiation	
Transcription factors	
AscH	Overexpression generates oligodendrocytes
	Expressed in NSCs to produce GABAergic interneurons in OB
	Expressed in NSCs to produce glutamatergic neurons in hippocampus
Neurog2	Expressed in NSCs to produce glutamatergic neurons in hippocampus
	Expressed in NSCs to produce glutamatergic neurons in svz
Tbr2	Expressed in NSCs to produce glutamatergic neurons in svz
Epigenetic mechanisms	
Gadd45b	Necessary for dendritic arborization
MBD1	Necessary for neuronal differentiation
MeCP2	Necessary for neuronal maturation
Mll1	Necessary for neuronal differentiation in svz
Migration	
IGF-1	Necessary for neuroblast migration
Shh	Necessary for neuroblast migration
Integration	
Extrinsic factors	
BDNF	Increases neuronal survival and dendritic arborization
FGF-2	Necessary for synaptic plasticity
GABA	Necessary for dendritic arborization and synapse formation
Glutamate	Necessary for neuronal survival and synaptic plasticity
NT-3	Necessary for synaptic plasticity
Intrinsic factors	
Cdk	Necessary for neuronal survival and dendritic arborization
CREB	Increases neuronal survival and dendritic arborization
DISC1	Decreases synaptic integration
Klf-9	Increases synaptic integration
NeuroDl	Necessary for neuronal survival and maturation

Source: Mu, Yangling, Star W Lee, and Fred H Gage. "Signaling in Adult Neurogenesis." *Current Opinion in Neurobiology* 20, no. 4 (August 2010): 416–23.

Figure 11: Molecular control of adult neurogenesis

Wnt Signaling Regulates Adult Hippocampal Neurogenesis

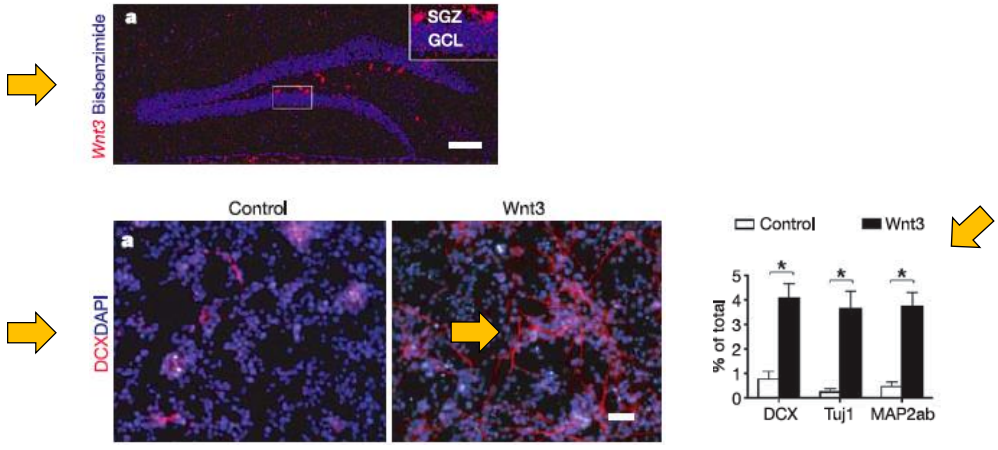

Figure 12: Wnt signalling

Adult NSC treated with Wnt factors differentiate into neurons

Source: Lie, Dieter-Chichung, Sophia A. Colamarino, Hong-Jun Song, Laurent Désiré, Helena Mira, Antonella Consiglio, Edward S. Lein, et al. "Wnt Signalling Regulates Adult Hippocampal Neurogenesis." *Nature* 437, no. 7063 (October 27, 2005): 1370–75.

Molecular control of adult neurogenesis

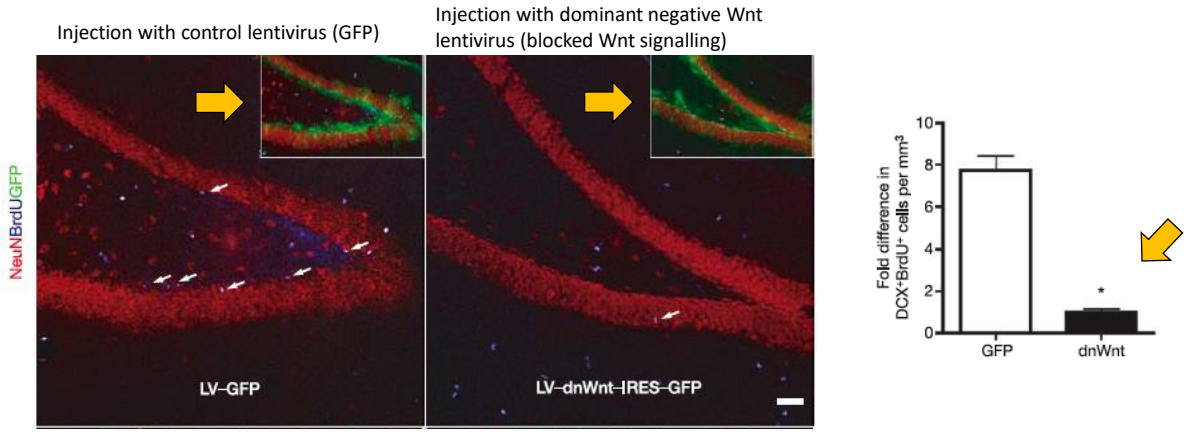

Figure 13: Molecular control of adult neurogenesis

Blockade of Wnt signalling reduces adult hippocampal neurogenesis

Functionality of Adult Neurogenesis

Level of Neurogenesis in DG is positively correlated with hippocampal dependent learning tasks

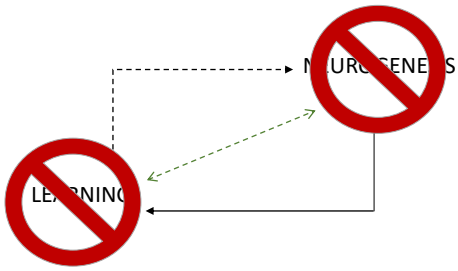

Figure 14: Learning and memory

New neurons

- Increase memory capacity
- Reduce interference between memories
- Or add information about time to memories
- OR forgetting

Functional Relevance of Adult Neurogenesis: Mood & Depression

Adult Neurogenesis is implicated in mood regulation & depression

- Neurogenesis is reduced in animal models of depression
- Many treatments for depression promote Neurogenesis
- Even though Neurogenesis alone cannot mediate the effect of antidepressants, it is a key player

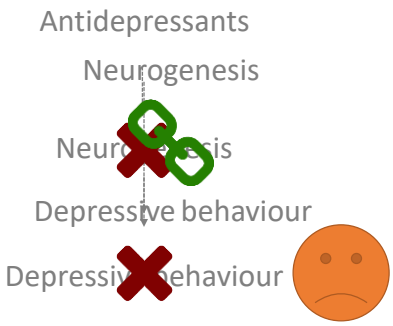

Figure 15: Mood and depression