Comparing ‘Gene X’ expression in mouse and human using Allen Brain Atlas & Brain Explorer: in search of a common network

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What do we know about ‘Gene X’ so far?

- KO mouse shows enhanced cognitive function
- Relatively high expression in the CNS, less in the periphery

My interest: translational research, MoA, biomarker

- Translational research: Are mice and human comparable?
  In drug development, we often use an animal model of human disease. Therefore, it is important to see if our target functions similarly across the species.
  -> comparison of gene expression in mouse and human CNS using Allen (Developing) Mouse and Human Atlases
- MoA and BM: What is the function of the ‘gene X’ and how it improves cognition? How do we know if our drug is modulating ‘gene X’?
  Afferent and efferent areas of the region with high ‘gene X’ expression may give us some clues about its function and possibly its biomarkers.
  -> Allen Mouse Connectivity Atlas + literature search

1. Gene Expression pattern comparison

A1. Human development

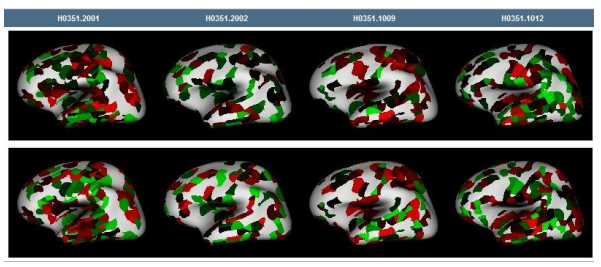
- 9 pcw: **dorsal thalamus**
- 13 pcw: **mediodorsal nucleus of thalamus**
- 16 pcw: STR, **mediodorsal nucleus of thalamus** (consistent in 3 donors)
- 17-24 pcw: **mediodorsal nucleus of thalamus**, STR

(birth)

- 1 yr: STR, DLPFC, VLPFC, ACC
- 8 yr: DLPFC, A1C, STC, amygdaloid complex NOT in cerebellum
- 15 yr: OFC, **mediodorsal nucleus of thalamus**, amygdaloid complex, STR NOT in cerebellum
- 19 yr: VLPFC, A1C, amygdaloid complex, STR NOT in cerebellum
- 21 yr: DLPFC, ACC NOT in cerebellum
- 30 yr: ACC NOT in cerebellum
- 36 yr: ACC, amygdaloid complex NOT in cerebellum

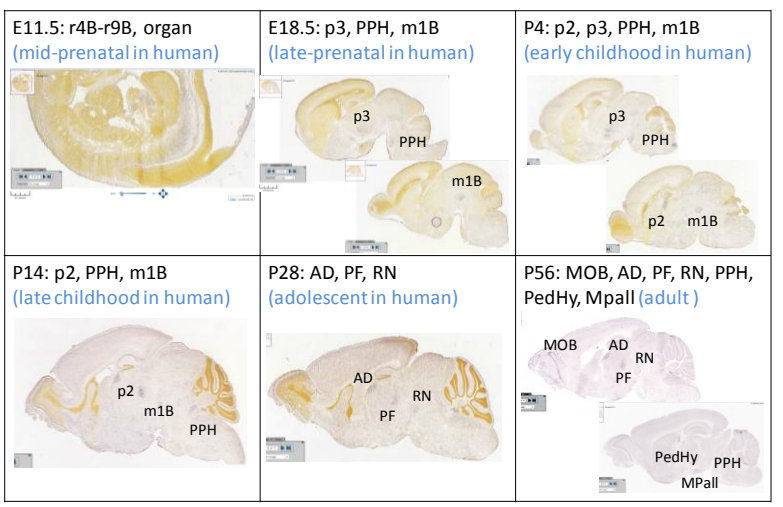
NB: 16 brain regions were looked at + some brain regions had not data (and this does not mean the missing region did not express ‘Gene X’)
Our WB data from an adult human showed protein expression in the: prefrontal, hippocampus and amygdala and NOT in cerebellum and thalamus (striatum was not looked at)

A2. Adult human (n = 4)

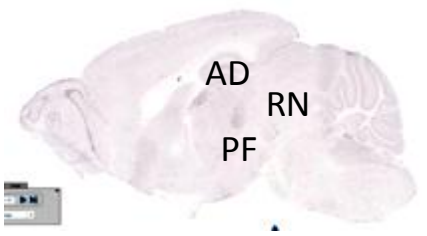


4 out of 4: Globus pallidus
3 out of 4: **mammillary body**, medial parabrachial nucleus, posterior hypothalamic area, preoptic region, **red nucleus**
2 out of 4: central grey substance of midbrain, **central nucleus of the amygdala**, **cingulate gyrus**, …

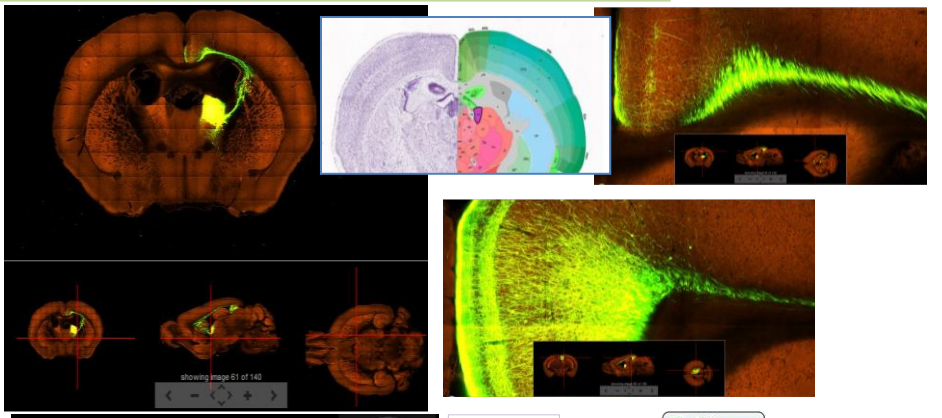
B. Mouse



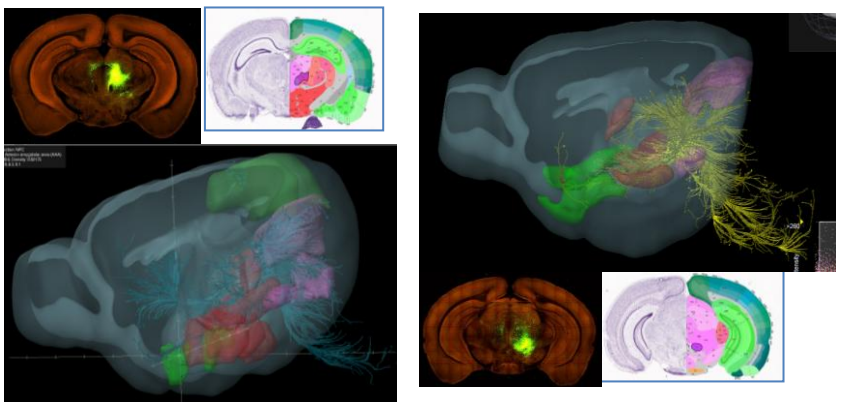
2. The networks of brain regions expressing ‘Gene X’



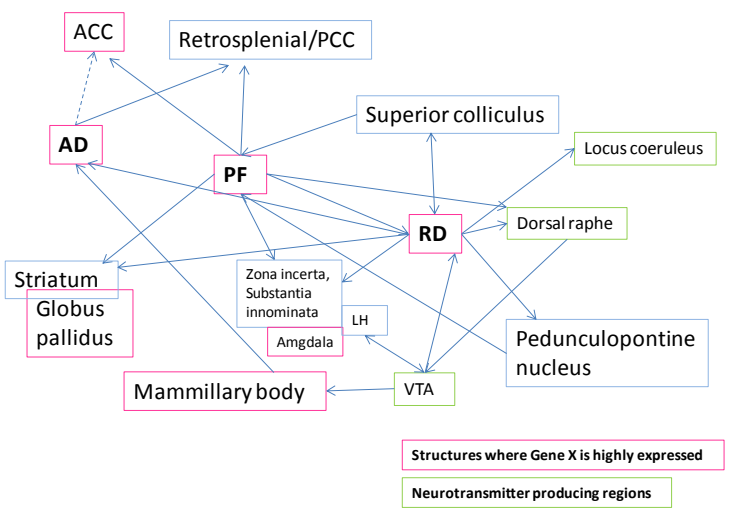
Anterodorsal thalamic nucleus (AD): Papez circuit



Parafascicular Nucleus (PF) & Red nucleus (RN)



Summary



Next steps…

- Neurochemical and functional properties of the networks
- Gene correlation analyses to search for potential BMs