Gene Z and the Mouse Prefrontal Cortex - Enoch Ng (UToronto)

Introduction

Gene Z is upregulated in the prefrontal cortex of individuals who had major neuropsychiatric diseases. It is an open question whether the upregulation is part of the disease process or a compensatory effect. One way to address this question is to overexpress Z in an analogous region in the mouse brain and test for phenotypes relevant to neuropsychiatric disease. The prefrontal cortex can be defined as the major projection area of the mediodorsal nucleus of the thalamus. However most of our knowledge of mouse prefrontal cortex has been extrapolated from rats and few tracing studies have been performed to explore prefrontal connectivity in mice.

Objectives

1. Characterize Z expression in human prefrontal cortex.
2. Define the prefrontal cortex in the mouse and characterize Z expression there.
3. Characterize projection areas of the mouse prefrontal cortex relative to the rat.

Materials & Methods

The following Allen Brain Atlas resources were used:

ALLEN INSTITUTE for BRAIN SCIENCE
Fueling Discovery

Human Brain
A multi-modal, multi-resolution atlas detailing gene expression across the adult human brain

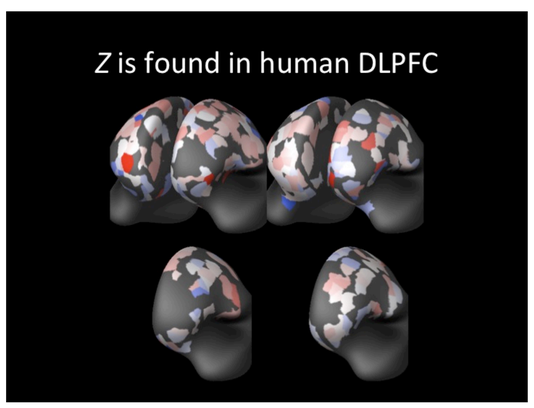
Developing Human Brain
A detailed atlas of gene expression across human brain development

Mouse Brain
A genome-wide, high-resolution atlas of gene expression throughout the adult mouse brain

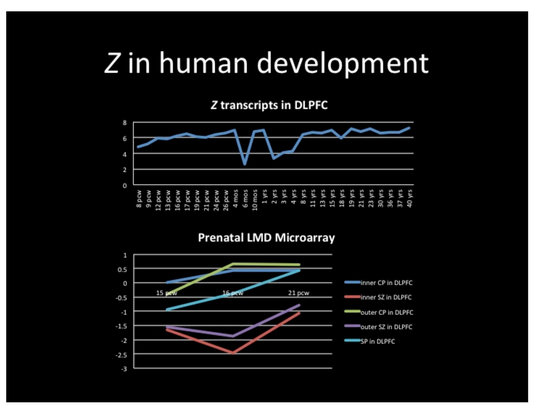
Mouse Connectivity
A high-resolution map of neural connections in the mouse brain

Results

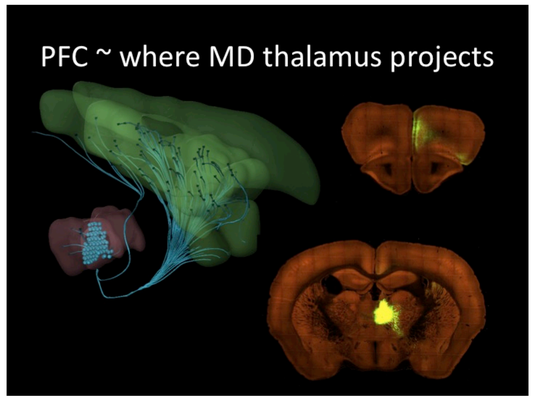
Z expression in the human and mouse prefrontal cortex.



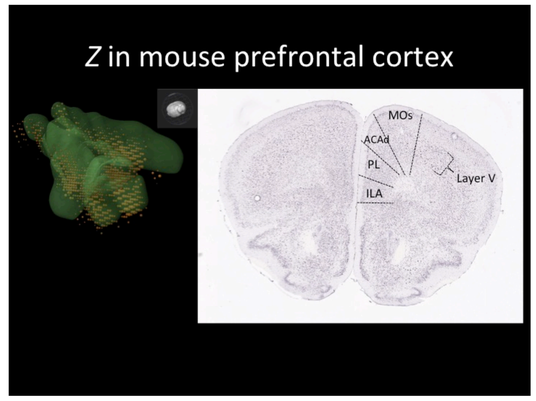
Human microarray data from 4 adult control subjects shows evidence of Z expression.



The developmental transcriptome and prenatal laser microdissection microarray datasets suggest Z is expressed throughout development in the dorsolaterla prefrontal cortex.

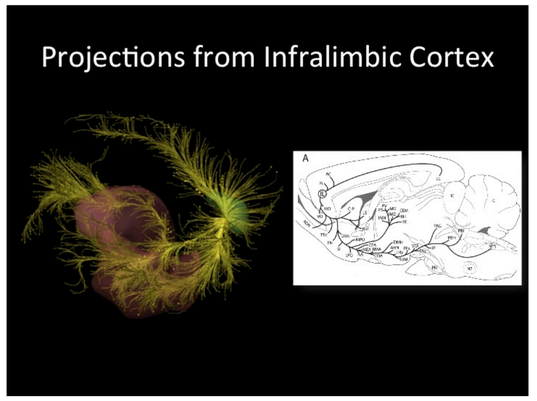


AAV injection into the mediodorsal nucleus of the thalamus shows major projections to infralimbic, prelimbic, and dorsal anterior cingulate cortices. (Mouse connectivity dataset experiment 114291646)

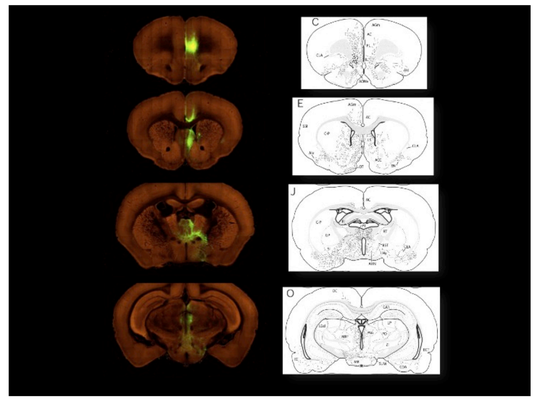


In situ hybridization shows Z is expressed throughout regions of the mouse prefrontal cortex (ILA = infralimbic area, PL = prelimbic area, ACAd = anterior cingulate area, dorsal part, MOs = secondary motor area).

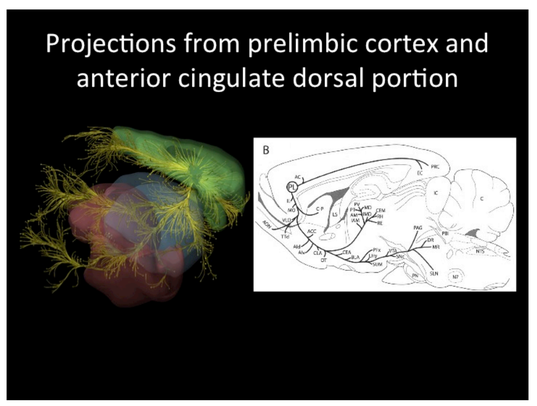
Comparing projections from the mouse prefrontal cortex with those in the rat



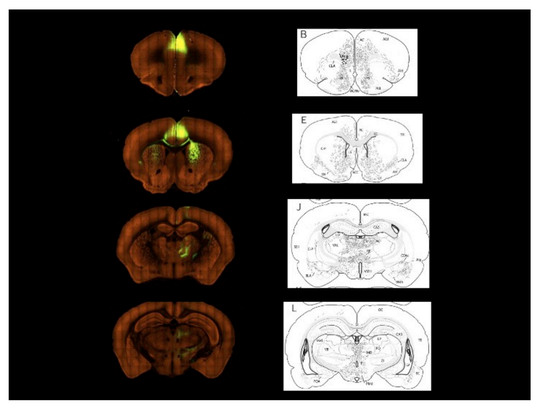
Left = projections from infralimbic cortex in the mouse (green = infralimbic area, pink = thalamus, red = hypothalamus) (Experiment 157556400). Right = major projections from infralimbic cortex in the rat from Vertes, 2004.



Left = projections from mouse infralimbic cortex. Right = projections from rat infralimbic cortex (from Vertes, 2004).



Left = projections from anterior cingulate and prelimbic areas in the mouse (green = anterior cingulate and prelimbic areas, blue = caudate putamen, pink = thalamus, red = hypothalamus) (Experiment 112458114). Right = major projections from prelimbic cortex in the rat from Vertes, 2004.



Left = projections from mouse anterior cingulate and prelimbic areas. Right = projections from rat prelimbic cortex (from Vertes, 2004).

Conclusions

Z is expressed throughout development in human dorsolateral prefrontal cortex. Z is expressed in mouse prefrontal cortex (as defined by the major projection sites of the mediodorsal nucleus of the thalamus). The mouse medial prefrontal cortex projects to similar structures as in the rat.

Reference: Vertes R (2004). Differential projections of the infralimbic and prelimbic cortex in the rat. *Synapse*. 51:32-58.