Proposed Outline for Thesis

1. Introduction

i. Introduce and situate the problem in context: how is specificity in neural circuitry established?

ii. Basics of axon guidance/chemoaffinity; including target-derived cues in visual and other systems, and intermediate target interactions/cues

iii. Evidence from other systems that tract organization is an important component of circuit development

iv. Basics of visual system development in the mouse

v. Pose the question: Is there pre-target sorting of binocular RGC axons in the mouse OT?

vi. Review literature of visual system axon order (topographic, age-specific, etc.)

vii. Outline project

2. Eye-specific organization of RGC axons in the developing mouse optic tract

i. Whole-eye tract labeling experiments at different ages

ii. Eye-specific organization is distinct from topographic organization in the tract (VT/VT)

iii. Ipsi axons are segregated in the nerve (evidence from SERT-Cre-GFP or zsgreen mice)

iv. *Description of glia in relation to ipsi and contra axon cohorts?*

*v. EM of the tract?*

3. Fasciculation Behavior of ipsi and contra axons

i. Higher resolution images of ipsi and contra fibers from tract labeling experiments provide suggestions of fasciculation (but also indicate that it is incomplete)

ii. In vitro approach: describe assay

iii. VT neurites have a greater tendency to self-fasciculate in vitro and do so for longer distances than contras

iv. Data from culture experiments with chiasm cells

v. A note on the potential for this assay to be used to test other candidate molecules (from Qing’s microarray) (brief here, more thorough in appendix)

4. A role for EphB1 in tract organization and fasciculation

i. Intro to EphB1 – past findings on targeting; other work on Eph/ephrins in fasciculation

ii. Aberrant fasciculation of remaining ipsi fibers in the tract of EphB1-/- mice (in vivo tract labeling data)

iii. Data and analysis of in vitro EphB1/wt and EphB1/EphB1 co-culture experiments: a role for EphB1 in fasciculation behavior of ipsi neurites?

5. Discussion and Conclusions

6. Materials and Methods

7. Appendix I: Eye-specific tract organization in other mutants

i. PlexinA1

ii. Tag1

iii. Protocadherin tri-cluster mutants

iv. Linx

8. Appendix II: ClearT and ClearT2 work

9. Appendix III: Alternative approaches to the in vitro assay