NAME, POSITION, ACADEMIC DEPARTMENT

Mark Zervas
Manning Assistant Professor of Biology
Department of Molecular Biology, Cell Biology and Biochemistry
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EDUCATION

1996-2000	Ph. D. Neuroscience* Albert Einstein College of Medicine
1993-1996	M.S. Neuroscience Albert Einstein College of Medicine
1989-1993	B.S. Chemistry University of Massachusetts at Boston

*Ph.D. dissertation: *Ganglioside Expression and Function in Development and Disease*.

The thesis findings provide insight into the differentiation of neocortical pyramidal neurons during brain development and the cellular pathology underlying Niemann-Pick Disease Type C (NPC). It also describes a therapeutic approach to ameliorate the neuropathology of NPC. Advisor: Dr. S.U. Walkley, DVM, Ph.D.. Note: This therapeutic approach has now been used for over ten years to ameliorate disease phenotypes in children with NPC.

PROFESSIONAL APPOINTMENTS

2006-Present	Brown University Assistant Professor of Biology, tenure track Department of Molecular Biology, Cell Biology, and Biochemistry
2006-Present	Brown University Neuroscience Trainer Department of Neuroscience
2000-2006	NYU School of Medicine Postdoctoral Fellow Skirball Institute for BioMolecular Medicine

ACADEMIC HONORS

Fellowships

2003-2006	Ruth L. Kirschstein National Research Service Award, NIH (F32HD43533)
1995-1998	NIH Pre-Doctoral training grant fellowship, Albert Einstein College of Medicine (NS07098).

Honors

2006-Present	Manning Assistant Professorship
2011	Invited Honorary Lecturer at 8th Annual Pharmacology Graduate Students Symposium, Stony Brook University
2011	Invited organizer of the Northeast Regional Meeting of the Society for Developmental Biology
2010	Richard B. Salomon Faculty Research Award
2009	Tuberous Sclerosis Research Conference Travel Award
2007	The Rhode Island Foundation Medical Research Award
2007	Brown University Brain Science Program Pilot Research Grant
2000	Thesis Departmental Honors, Albert Einstein College of Medicine
1997	Department of Neuroscience Travel Award, Albert Einstein College of Medicine

COMPLETED PUBLICATIONS

Work completed at Brown University are indicated by blue numbers

1. Ellisor D, Rieser C[i], Voelcker B[ii], **Zervas M*** (2012) Genetic Dissection of Midbrain Dopamine Neuron Development in vivo. *Dev Biol* 372:249-262 (PMID: 23041116).

The major finding in this manuscript is that we uncovered a signaling molecule that is required for a dopamine neuron subtype. This manuscript describes how a point mutation in Wnt1 causes a complete loss of medial (ventral tegmental area) dopamine neurons while relatively sparing bilateral (substantia nigra) dopamine neurons. In addition, this manuscript describes that the phenotype results from a previously unappreciated late role of Wnt1 in establishing dopamine neuron subpopulations. We showed that mice with the point mutation in Wnt1 have an altered molecular hierarchy. We also used conditional gene deletion experiments and removed genes affected by the point mutation, which showed that the phenotype was unique to Wnt1 function. Our analysis uncovered specific temporal roles for the engrailed genes and Fgf8 in dopamine neuron development. Finally we showed a species-specific function of the mouse, but not drosophila, engrailed genes in the induction of dopamine neurons. This work was carried out completely in my lab at Brown University. MZ wrote the manuscript.

[i]The second author (C. Rieser) was an undergraduate conducting independent research and her senior honors thesis work in my lab. [ii]The third author (B. Voelcker) is a current undergraduate student that contributed to this manuscript.

Corresponding Author

2. Hagan N‡, **Zervas M*** (2012) *Wnt1* expression temporally allocates upper rhombic lip progenitors and defines their terminal cell fate in the cerebellum. *Mol Cell Neurosci* 49:217-229 (PMCID: PMC3351839).

The major finding in this manuscript is that we show that the Wnt1 genetic lineage temporally and spatially generates cell types in the cerebellum. This paper describes the molecular identity of Wnt1-expressing progenitors positioned in an embryonic germinal zone, the rhombic lip. Using both short term lineage tracing and genetic inducible fate mapping we showed how the Wnt1 lineage in the rhombic lip, marked at specific time points during embryogenesis, differentially contributes to the developing and adult cerebellum. This manuscript is also one of the first to couple genetic inducible fate mapping and neural circuit tracing to show that the Wnt1 lineage in two spatially disparate regions are functionally connect during development suggesting that genetic lineage may be used to functionally bind anatomically discrete regions. This work was carried out completely in my lab at Brown University. NH and MZ wrote the manuscript.

‡The primary author (N. Hagan) was a graduate student in the Brown Neuroscience Graduate Program and this work comprised a portion of her Ph.D. thesis requirements.

Corresponding Author

3. Brown A‡, Machan JT, Hayes L, **Zervas M*** (2011) Molecular organization and timing of *Wnt1* expression define cohorts of midbrain dopamine neuron progenitors *in vivo*. *J Comp Neurol* 519:2978-3000 (PMCID: PMC3359795).

The major finding in this manuscript is that we show for the first time how the Wnt1 lineage contributes to dopamine neurons in a temporally specific manner. This paper describes the molecular identity of Wnt1-expressing progenitors positioned in the ventral midbrain primordia. We described a novel transgenic line to show that the molecular identity of midbrain dopamine neuron progenitors dynamically changes during critical stages of dopamine neuron specification and differentiation. We also used genetic inducible fate mapping to show that the Wnt1 lineage is progressively restricted in non-dopamine neuron populations during a short time window. In contrast, the Wnt1 lineage continues to give rise to dopamine neurons in the ventral tegmental area and substantia nigra during two temporal epochs of contribution. This manuscript is the first to link molecularly distinct Wnt1-expressing progenitors and timing of gene expression to the dopamine system. This article taken together with its companion article (#4 below) shows how Wnt1, Shh, and Gli1 lineages differentially shape the complex dopamine neuron anatomy. This work was carried out completely in my lab at Brown University. AB and MZ wrote the manuscript.

‡The primary author (A. Brown) was a graduate student in the Brown Neuroscience Graduate Program and this work comprises a portion of her Ph.D. thesis requirements.

Corresponding Author

4. Hayes L‡, Zhang Z, Albert P, **Zervas M***, Ahn S* (2011) The timing of Sonic Hedgehog and Gli1 expression segregates midbrain dopamine neurons. *J Comp Neurol* 519:3001-3018 (PMCID: PMC3154975).

The major finding in this manuscript is that Shh-expressing and Shh-responding cells contribute to dopamine neuron diversity in distinct temporal windows. This paper describes the molecular identity of Shh-expressing and Shh-responding (Gli1-expressing) progenitors positioned in the ventral midbrain primordia. We used genetic inducible fate

mapping to show that these lineages contribute to dopamine neuron subtypes depending on the stage that either express Shh or respond to Shh signaling in vivo. This manuscript is the first to link temporally changing progenitors that are coincidentally and functionally responding to a signaling molecule. This manuscript showed for the first time that progenitors in the caudal midbrain primordia contribute to the ventral tegmental area dopamine neurons during a short temporal window. LH conducted the experiments in the Ahn lab. SA and MZ contributed equally to advising, mentoring, experimental design, and analysis. LH, SA, and MZ wrote the manuscript.

‡The primary author (L. Hayes) was a graduate student in the Brown Neuroscience Graduate Program and this work comprised a portion of her Ph.D. thesis requirements.

Co-corresponding author

5. Luu B‡, Ellisor D, **Zervas M*** (2011) The Lineage Contribution and Role of *Gbx2* in Spinal Cord Development. *PLoS ONE* 6(6): e20940. doi:10.1371/ journal.pone.0020940 (PMCID: PMC3116860).

The major finding in this manuscript is that the timing and duration of Gbx2 expression delineates the terminal fate of spinal cord neurons. This paper fully characterizes the molecular identity of the Gbx2-expressing progenitors in the spinal cord. Notably, we showed that the molecular Gbx2 code changes dynamically over time. The lineage derived from these progenitors contributes to dorsal-ventral cell types in the context of time and changes in waves along the rostral-caudal axis of the spinal cord. We used long term genetic inducible fate mapping and showed that the timing of Gbx2 expression in progenitors delineates the terminal fate of dorsal spinal cord. We also showed that the temporal deletion of Gbx2 alters the molecular identity of the developing cord, disrupts the lineage contribution and distribution of terminally differentiated spinal cord neurons. This work was carried out completely in my lab at Brown University. BL and MZ wrote the paper.

‡The first author (B. Luu) was an undergraduate conducting independent research and his senior honors thesis work in my lab and directly led to this paper.

Corresponding Author

6. Ellisor D, **Zervas, M*** (2010) Tamoxifen dose response and conditional cell marking: Is there control? *Mol Cell Neurosci* 45:132-138 (PMID: 20600933). Selected scientific image featured on cover.

The major finding in this manuscript is that we show that tamoxifen does not linearly control the extent of recombination in a highly controlled, quantitative analysis. There has been a dogma associated with CreER/loxP technology which is that the extent of recombination of a population of neurons can very tightly controlled by tamoxifen dose. This is an important concept related to lineage mapping and perhaps more seminal to condition gene deletion strategies using CreER mouse lines. Thus we sought to address this issue by conducting a rigorous tamoxifen dose response study using our well characterized Wnt1-CreER mouse line in and a conditional reporter allele (mGFP). We used an automated quantification approach to count the number of recombined cells in the trigeminal ganglia and showed tamoxifen dose (50mg/kg-500mg/kg) did not control the extent of recombination. Thus, we provide valuable information in this paper for the mouse community to draw from and to use in designing experiments. This work was carried out completely in my lab at Brown University. DE and MZ wrote the paper.

Corresponding Author

7. Brown A[Δ], Brown S[Δ], Ellisor D[Δ], Hagan N[Δ], Normand E[Δ], **Zervas, M*** (2009) A Practical Approach to Genetic Inducible Fate Mapping: A Visual Guide to Mark and Track Cells *In Vivo*. *J Vis Exp*, 43**:** pii: 1687, doi: 10.3791/1687 (PMCID: PMC2846818).

The major finding in this manuscript is that we provide a comprehensive guide to conduct genetic lineage mapping studies in vivo. Genetic inducible fate mapping and conditional gene deletion is a rapidly advancing approach to unravel complex problems in developmental biology and in disease. My lab has a strong expertise in the concepts and technical methodology of this approach and its application. We therefore provide an easy to follow guide to conduct lineage tracing experiments, embryonic micro-dissections, and adult tissue preparation, and analysis of lineage mapping. MZ conceived of the experimental design and produced the manuscript and video article.

[Δ]These authors contribute equally to this paper.

Corresponding Author

8. Ellisor D, Koveal D, Hagan N[‡], Brown A[‡], **Zervas M*** (2009) Comparative analysis of conditional reporter alleles in the developing embryo and embryonic nervous system. *Gene Expr Patterns,* 9:475-489 (PMCID: PMC2855890).

The major finding in this manuscript is that the Wnt1 and En1 lineage derivatives have a complex interplay in establishing tissues and contribute to distinct neural circuits. This paper described an extensive analysis of three commonly used conditional reporter alleles (R26R, Z/EG, mGFP) with a goal of exploiting their strengths to uncover distinct aspects of lineage contribution. We conducted these experiments with an emphasis on developing neural crest derivatives of the Wnt1 and En1 lineages. We demonstrated how these lineages were distributed in proliferating ventricular zones and subsequently in differentiating zones. We also described neural circuits related to lineage-derived neurons: 1. The trigeminal ganglia and its connections from the whisker placodes to the brainstem; 2. Spinal cord dorsal root ganglia and their projections to the lateral body wall. We clarified how these lineages contributed to specific structures. This work was carried out completely in my lab at Brown University. DE and MZ wrote the paper.

[‡]These authors were graduate students in the lab that contributed to this paper.

Corresponding Author

9. **Zervas M*** (2007) Genetics, Neurobiology, and Translational Medicine: The Future of Schizophrenia Research. *White Paper, Johnson & Johnson Pharmaceutical Research and Development*. 133pp.

The major finding in this white paper is that schizophrenia would benefit from a deeper understanding how the dopamine neuron subtypes are established, maintained, and affected in dopamine related diseases. Schizophrenia is obviously an incredibly complex disorder and the front line drugs from Johnson and Johnson that target the dopamine system were in need of evaluation to decide on a forward moving strategy to augment their at the time current pharmaceuticals. I was asked to provide an unbiased assessment of the dopamine neuron circuits and genetic underpinnings of dopamine neuron diversity with a challenge to describe novel approaches to target drugs to subsets of dopamine neurons. I described novel approaches to target specific small molecules to selective sets of dopamine neurons with an emphasis on targeting the medial ventral tegmental area dopamine neurons. MZ researched and wrote the paper.

Researcher and Corresponding Author

10. Joyner AJ, **Zervas M** (2006) Genetic inducible fate mapping in mouse: establishing genetic lineages and defining genetic neuroanatomy in the nervous system. *Dev Dynamics* 235:2376-2385 (PMID: 16871622).

11. **Zervas M**, Blaess S, Joyner AJ (2005) Classical embryological studies and modern genetic analysis of midbrain and cerebellum development. *Curr Topics Dev Biol (Neural Development)*, 69:101-138. Invited review; Selected scientific image featured on cover (PMID: 16118800).

12. **Zervas M**, Opitz T, Edelmann W, Wainer B, Kucherlapati R, Stanton P (2005) Impaired Hippocampal Long-Term Potentiation (LTP) in Microtubule-Associated Protein 1B-deficient Mice. *J Neurosci Res* 82:83-92 (PMID: 16243598).

13. **Zervas M**, Millet S, Ahn S, Joyner AJ (2004) Cell behaviors and genetic lineages of the mesencephalon and rhombomere 1. *Neuron* 43:345-357 (PMID: 15294143).

14. **Zervas M**, Somers KL, Thrall MA, Walkley SU (2001) Critical role for glycosphingolipids in Niemann-Pick disease type C. *Curr Biol* 11(16):1283-1287 (PMID: 11525744).

15. **Zervas M**, Dobrenis K, Walkley SU (2001) Neurons in Niemann-Pick disease type C accumulate gangliosides as well as unesterified cholesterol and undergo dendritic and axonal alterations. *J Neuropathol Exp Neurol* 60(1):49-64 (PMID: 11202175).

16. Walkley SU, **Zervas M**, Wiseman S (2000) Gangliosides as modulators of dendritogenesis in normal and storage disease-affected pyramidal neurons. *Cerebral Cortex* 10(10):1028-1037 (PMID: 11007553).

17. **Zervas M** and Walkley SU (1999) Ferret pyramidal cell dendritogenesis: changes in morphology and ganglioside expression during cortical development. *J Comp Neurol* 413(3): 429-448 (PMID: 10502250).

18. Walkley SU, Siegel DA, Dobrenis K, **Zervas M** (1998) GM2 ganglioside as a regulator of pyramidal neuron dendritogenesis. *Annals of the NY Academy of Science* 845:188-199 (PMID: 9668352).

19. Edelmann W, **Zervas M**, Costello P, Roback L, Fischer I, Hammarback JA, Cowan N, Davies P, Wainer B, Kucherlapati R (1996) Neuronal abnormalities in microtubule-associated protein 1B mutant mice. *Proc Natl Acad Sci* USA 93:1270-1275 (PMCID: PMC40069).

PUBLICATIONS SUBMITTED OR PREPARED

Work completed at Brown University are indicated by bold blue numbers

1. Yang J[Δ,i], Brown A[Δ,‡], Ellisor D, Paul E, Hagan N, **Zervas M*** (2012). The dynamic temporal requirement of *Wnt1* in midbrain dopamine neuron development. *Development*, MS ID#: DEVELOP/2012/080630, Revision Under Review.

The major finding in this manuscript describes the temporal role of Wnt1 and its early role transcriptional regulation and its late role in controlling cell cycle exit. This paper describes a novel conditional allele of Wnt1 that we generated through recombineering

and used with specific Cre or CreER recombinase lines and conditional reporter alleles. Collectively, this approach showed that Wnt1 has an early role in regulating the transcription factor Lmx1a and is necessary for the development of all dopamine neurons. Subsequently, dopamine neuron progenitors still require Wnt1 but it no longer regulates Lmx1a, but rather controls the cell cycle of dopamine neuron progenitors. The later deletion of Wnt1 causes a premature exiting of the cell cycle, which is specific to dopamine neuron progenitors. The resulting disruption of dopamine neurons is characterized by the loss of medial dopamine neurons and an expanse of lateral dopamine neurons. Thus, we show that Wnt1 couples cell cycle and cell fate to contribute to dopamine neuron diversity. This work was carried out completely in my lab at Brown University. JY, AB, DE, EP, and MZ wrote the paper.

[Δ]These authors contribute equally to this paper. [i]The first author (J. Yang) was a postdoctoral fellow in my lab and generated the conditional Wnt1 allele; [‡]The co-first author (A. Brown) is a graduate student in the Brown Neuroscience Graduate Program and this work comprises a portion of her Ph.D. thesis requirements; AB was responsible for the experimental design and cell cycle analysis that contributed to this paper.

Corresponding Author

2. Normand E[‡], Browning C[i], Machan JT, Voelcker B[ii], Thorne C[iii], Murphy E[iii], Moore C[iii], **Zervas M[iii,*]** (2012) Seizures and compulsive grooming behaviors resulting from thalamus-specific *Tsc1* gene inactivation. Neuron, Manuscript #NEURON-D-12-01342, Under revision.

The major finding in this manuscript is that the temporal deletion of Tsc1 and mTOR dysregulation in the thalamus disrupts thalamocortical circuit development and causes repetitive grooming abnormalities and seizures. This paper uses a combination of conditional gene deletion and genetic inducible fate mapping and genetic lineage analysis to show that Tsc1 deletion in the embryonic thalamus disrupts the neural circuitry connecting the thalamus to the cerebral cortex. Specifically, we showed that somatosensory cortex was disrupted and that thalamic axons did not properly innervate the and layer 4 barrels. Notably, the disruption caused a secondary patterning defect of the cortical target area. Behaviorally, the deletion of Tsc1 in the thalamus caused excessive grooming and robust, frequent, spontaneous seizures. I established a collaboration with Dr. Chris Moore's lab at Brown University where we used multi-array electrodes to show complex electrical disturbances that emanated from the thalamus and propagated across multiple cortical layers. The genetic, cellular, and circuit experiments were designed by EN and MZ and this work was carried out in my lab at Brown University. The physiology was designed by MZ and CM. EN and MZ wrote the manuscript.

[‡]The primary author (E. Normand) is a graduate student in the Brown Neuroscience Graduate Program and this work comprises a portion of her Ph.D. thesis requirements. [i]C. Browning was a high school student and [ii]B. Voelcker was an undergraduate that together made substantial contributions to this manuscript. [iii]C. Thorne, E. Murphy, and C. Moore and M. Zervas conducted and analyzed the electrophysiology data

Corresponding Author

3. Normand E[‡], Browning C[i], Hagan N[ii], **Zervas M*** (2012) The timing and duration of *Gbx2* expression delineates thalamocortical or dopamine medial forebrain bundle circuitry. *Gene Expr Patterns*, Manuscript #MODGEP1128, Under revision.

The major finding in this manuscript is that progenitors that expressed gbx2 during a single short temporal epoch contributed to dopamine neurons that axons that comprised the medial forebrain bundle. This manuscript is the first to show that dopamine neurons are derived from the progenitors that transiently express Gbx2 only during a twenty-four window. In contrast, thalamic progenitors express Gbx2 for a more prolonged time period and contribute to the thalamic neurons and their axons that extend above the medial forebrain bundle. We show that two parallel sets of neural circuits derived from the same lineage but with different temporal dynamics establish closely traversing yet separate axonal tracts. This work was carried out completely in my lab at Brown University. EN and MZ wrote the manuscript.

[‡]The primary author (E. Normand) is a graduate student in the Brown Neuroscience Graduate Program and this work comprises a portion of her Ph.D. thesis requirements. [i]C. Browning was a high school student and [ii]N. Hagan was a graduate student who contributed to this manuscript.

***Corresponding Author**

4. Brown S[‡], **Zervas M*** (2012) Temporal expression of *Wnt1* defines the competency state and terminal identity of auditory progenitors in the developing cochlear nucleus and inferior colliculus. *Neural Dev,* In Preparation.

The major finding in this manuscript is that Wnt1-expressing progenitors in the auditory hindbrain contribute to contralateral projecting auditory neurons. This paper describes the use of long term lineage analysis and mutant phenotypes to delineate the role of Wnt1 in establishing specific types of projection neurons in the auditory nuclei of the brainstem. This work was carried out completely in my lab at Brown University. SB and MZ wrote the manuscript.

[‡]The primary author (S. Brown) was a graduate student in the Brown MCB Graduate Program and this work comprised a portion of his Ph.D. thesis requirements.

***Corresponding Author**

5. Hagan N[Δ,‡], Guarante J[Δ,i], **Zervas M*** (2012) The contribution of the *Gbx2* lineage to the adult cerebellum. *Neural Dev*, In Preparation.

The major finding in this manuscript is that the Gbx2 lineage contributed to the distinct cell types and functionally discrete regions of the cerebellum based on the timing of gene expression. This paper describes the use of long term lineage analysis to delineate how Gbx2-expressing progenitors contribute to and are distributed in cohorts of specific types of neurons in the cerebellum and in the pre-cerebellar system. This work was carried out completely in my lab at Brown University. NH, JG, and MZ wrote the manuscript.

[Δ]These authors contribute equally to this paper. [‡]The primary author (N. Hagan) was a graduate student in the Brown Neuroscience Graduate Program and this work comprised a portion of her Ph.D. thesis requirements. [i]The co-first author was an undergraduate conducting independent research and her senior honors thesis work in my lab and this work comprised her senior honors thesis.

***Corresponding Author**

INVITED LECTURES

Invitations since joining Brown University are indicated by bold blue numbers

1. Harvard University Medical School, Departmental Seminar Series
Cambridge MA, November 8, 2012

Delineating a temporal window of Tsc1 requirement for proper thalamus development and function

2. University of Connecticut Health Center, Department of Neuroscience Seminar Series
Farmington CT, September 25, 2012
Temporal and mosaic disruption of Tsc1 causes abnormal thalamocortical circuitry and complex behaviors in murine Tuberous Sclerosis

3. Brandeis University, Neurobiology Journal Club
Waltham MA, September 11, 2012

Temporal and mosaic disruption of Tsc1 causes abnormal thalamocortical circuitry and complex behaviors in murine Tuberous Sclerosis

4. University of Massachusetts Amherst, Departmental Seminar Series
Amherst MA, February 22, 2012

Genetic Approaches in Mouse to Interrogate Brain Development and Disease

5. Stony Brook University, 8th Annual Pharmacology Graduate Students' Symposium
Stony Brook NY, June 6, 2011

Determining how the temporal and spatial deletion of Tsc1 and mTOR dysregulation during brain development causes neurological disease in Tuberous Sclerosis

Honorary Lecture, Invited by Graduate Students

6. Northeast Regional Meeting of the Society for Developmental Biology
Woods Hole MA, March 25-27, 2011

Opening Remarks: Development and diversity in multiple species

7. Brown University, Cancer Collaborative Research Opportunities Symposium
Providence RI, February 2, 2011

Using Novel Genetic Approaches In Mice To Dissect The mTOR Pathway in Development and Disease

8. National Institutes of Health, NIH Graduate Student Seminar Series
Bethesda MD, December 14, 2010

Determining the Temporal Role of Tsc1 in The Development of The Thalamus: Alterations in Thalamic Neurons, Thalamocortical Circuits, and Behavior in a Novel Mouse Model of Tuberous Sclerosis

Invited by graduate students

9. Albert Einstein College of Medicine, Dominick P. Purpura Neuroscience Seminar series
Bronx NY, November 10, 2010

Determining The Temporal Role of Tsc1 in The Development of The Thalamus: Alterations in thalamic Neurons, Thalamocortical Circuits, and Behavior in a Novel Mouse Model of Tuberous Sclerosis

10. Vartan Gregorian Elementary School, Vartan Gregorian Science Conference
Providence RI June 11, 2010

Can An Animal Grow New Limbs?

Invited to teach elementary students about stem cells and limb regeneration in axolotls

11. Women & Infant's Hospital of Rhode Island, Pediatric Research Colloquium
Providence RI, May 14, 2010

Tsc1 Conditional Deletion in Embryonic Thalamus and Brain Pathology: Investigating Salient Features of the Human Developmental Genetic Disorder Tuberous Sclerosis Using Mouse Genetic Approaches

12. North-East Regional Meeting of the Society of Developmental Biology
Woods Hole MA, April 23-25, 2010

The Lineage Contribution and Role of the Transcription Factor Gbx2 in Spinal Cord Development in vivo

13. Brown University, Nanoscience & Neuroscience Workshop
Providence RI, September 28, 2009

Coupling Genetic Approaches and Nanotechnology to Mark and Track Cell Lineages in vivo

14. 2009 International TSC Research Conference
Bloomingdale, IL, September 23-26, 2009

Effects of Conditionally Inactivating Tsc1 in the Thalamus During Development in a Mouse Model of Tuberous Sclerosis

15. National Institute of Child Health and Human Development
Bethesda MD, October 07-08, 2008

Stereological Analysis of Midbrain Dopamine System

Invited to teach mini-course/seminar

16. National Institute of Health, Graduate Partnership Program retreat
Cumberland MD, Thursday, July 18, 2008

Project Design

17. National Institute of Health, Graduate Partnership Program retreat
Cumberland MD, Thursday July 17, 2008

Graduate School Roadmap

18. 2007 International TSC Research Symposium
Annapolis MD, September 23-25, 2007
Genetic Approaches to Study Cerebellum Development, Circuitry, and Disease

19. Cold Spring Harbor Labs, CSHL Stem Cell Course Lecture
Cold Spring Harbor NY, August 13, 2006
Genetic Lineage and Stem Cells: Linking Development, Disease, and Physiology of the Brain

20. National Institute of Child Health and Human Development, Departmental Seminar Series
Bethesda MD, June 06, 2006
Midbrain Development: Gene Regulation, Cell Behaviors and Establishing Dopaminergic Neurons in vivo

21. Pioneer Valley Life Science Institute/UMass Amherst, Departmental Seminar Series
Amherst MA, February 27, 2006
Development of the midbrain and cerebellum: gene regulation, cell behaviors, and establishing dopaminergic neurons in vivo

22. Brown University, MCB Departmental Seminar Series
Providence RI, February 14, 2006
Development of the midbrain and cerebellum: gene regulation, cell behaviors, and establishing dopaminergic neurons in vivo

23. Brandeis University, Departmental Seminar Series
Waltham MA, February 07, 2006
Development of the Midbrain: Gene Regulation, Cell Behaviors, and Establishing Dopaminergic Neurons

24. National Institute of Mental Health, Departmental Seminar Series
Bethesda MD, NIH, June 23, 2005
Development of the Midbrain: Gene Regulation, Cell Behaviors, and Establishing Dopaminergic Neurons

25. Maine Medical Center Research Institute, Departmental Seminar Series
Scarborough, ME, April 28, 2005
Genetic Lineage and Cell Behaviors During Midbrain/Hindbrain Development

26. National Institute of Child Health and Human Development, F32 Fellows Seminar Series
Bethesda MD, April 05, 2005
Genetic Lineage and Cell Behaviors During Midbrain/Hindbrain Development

27. The Niemann-Pick C Lesion & The Role of Intracellular Lipid Sorting in Human Disease (1st International Meeting)
Bethesda MD, October 14-16, 1999
Inhibition of Ganglioside Synthesis in Murine and Feline Models of Niemann-Pick Disease type C Ameliorates Neurological Disease

ABSTRACTS

All are since starting at Brown University in 2006

1. Brown A, Yang J, Ellisor D, and **Zervas M** (2012) The Dynamic Role of *Wnt1* in Midbrain Dopamine Neuron Progenitors in vivo. *Gordon Research Conference: Neural Development.* August 12-17, 2012, Salve Regina, RI.
   Poster Presentation by A. Brown

2. Normand E, Browning C, Machan JT, Voelcker B, **Zervas M** (2012) The deletion of *Tsc1* at specific developmental stages and in distinct regions of the thalamus disrupts neural circuit architecture and causes unique behavioral abnormalities. *Gordon Research Conference: Neural Development*. August 12-17, 2012, Salve Regina, RI.
   Poster Presentation by E. Normand

3. Normand E, Browning C, **Zervas M** (2012) Seizures and compulsive grooming behaviors resulting from thalamus-specific *Tsc1* gene inactivation. *Gordon Research Conference: Fragile X and Autism-related Disorders*. June 10-15, 2012, Stonehill College, MA.
   Poster Presentation by E. Normand

4. Ellisor D, Brown A, **Zervas M** (2012) Changing Temporal Requirements of *Wnt1* in Dopamine Neuron Development. IdEA Symposium: NIH, NIGMS Fourth Biennial National IDeA Symposium of Biomedical Research Excellence (NISBRE), June 27-27 2012, Washington, DC.
   Poster Presentation by D. Ellisor

5. Normand E, Browning C, **Zervas M** (2012) Cellular and behavioral consequences of mTOR pathway dysregulation within a population of subcortical neurons during mouse embryogenesis. Keystone Symposia: *Synapses and Circuits: From Formation to Disease*, Apr 1-6 2012, Steamboat Springs, Colorado.
   Poster Presentation by E. Normand
   Student travel award recipient

6. Normand E, **Zervas M** (2011) mTOR pathway dysregulation during thalamic development leads to severe behavioral abnormalities in adult mice. *Mammalian Development Meeting*. September 2, 2011, UCHC, CT. Student Presentation.
   Presentation by E. Normand

7. Rios M, Normand E, **Zervas M** (2011) The effects of rapamycin treatment on *Tsc1*-deficient neurons in the thalamus. *BP-ENDURE at Hunter/NYU Neuroscience Research* Symposium. July 29-31, 2011.
   Poster Presentation by M. Rios

8. Normand E, **Zervas M** (2011) Developmental and behavioral results of a Tsc1-null thalamus in an otherwise normal brain. *International TSC Research Conference: Summit for Drug Discovery in TSC and Related Disorders*. July 6-9, 2011, Washington DC.
   Poster Presentation by E. Normand
   Student travel award

9. Brown A, **Zervas M** (2011) Molecular organization and timing of *Wnt1* expression define cohorts of midbrain dopamine neuron progenitors *in vivo*. *Mammalian Development Meeting*.

September 2, 2011, UCHC, CT.
Poster Presentation by A. Brown

10. Brown A, **Zervas M** (2011) Molecular organization and timing of *Wnt1* expression define cohorts of midbrain dopamine neuron progenitors *in vivo*. *Northeast Regional Meeting of the Society for Developmental Biology.* March 25-27, 2011 Woods Hole, MA.
Poster Presentation by A. Brown
Best poster award

11. Normand E, **Zervas M** (2010) Conditional gene inactivation of *Tsc1* and cell marking in the thalamus reveals developmental alterations in a mouse model of Tuberous Sclerosis. *Gordon Research Conference: Neural Development*. August 15-20, 2010, Salve Regina, RI.
Poster Presentation by E. Normand

12. Brown A, **Zervas M** (2010) The contribution of the *Wnt1* lineage to midbrain dopaminergic neurons. *Gordon Research Conference: Neural Development*. August 15-20, 2010, Salve Regina, RI.
Poster Presentation by A. Brown

13. Normand E, **Zervas M** (2009) Effects of conditionally inactivating *Tsc1* in the thalamus during development in a mouse model of Tuberous Sclerosis. *International TSC Research Conference: from DNA to human therapies*. September 23-26, 2009, Bloomingdale, Illinois.
Poster Presentation by E. Normand

14. Luu B, **Zervas M** (2009) The lineage contribution and role of the transcription factor *Gbx2* in spinal cord development *in vivo*. *New England Science Symposium*. April 3, 2009, Harvard Medical School, Boston, MA.
Presentation by B. Luu

15. Hagan N, **Zervas M** (2009) The molecular Identity and Lineage of *Wnt1* Expressing Cells in the Cerebellum. *Mammalian Development Meeting*. May 15. 2009, U Mass Medical School.
Poster Presentation by N. Hagan

16. Brown S, **Zervas M** (2008) A novel transgenic reporter to mark and track specific lineages *in vivo*. *Society for Neuroscience* November 15-19, 2008, Washington DC.
Poster Presentation by S. Brown

17. Normand E, **Zervas M** (2008) Effects of conditionally inactivating Tsc1 on thalamo-cortical and midbrain circuitry and neuronal morphology during development in a mouse model of Tuberous Sclerosis. *Society for Neuroscience* November 15-19, 2008, Washington DC.
Poster Presentation by E. Normand

18. Hagan N, **Zervas M** (2008) The contribution of the *Wnt1* expressing cells to sub-populations and circuitry in the cerebellum. *Society for Neuroscience* Nov. 15-19, 2008, Washington DC.
Poster Presentation by N. Hagan

19. Ellisor D, **Zervas M** (2008) Comparative analysis of conditional reporter alleles in the embryonic nervous system. *Society for Neuroscience* November 15-19, 2008, Washington DC.
Poster Presentation by D. Ellisor

20. Hayes LN, **Zervas M**, Ahn S (2008) Sonic hedgehog signaling contributes to midbrain dopamine neuron development. *Soc Neurosci* November 15-19, 2008, Washington DC.
Poster Presentation by L. Hayes

21. Luu BF, **Zervas M** (2008) Genetic dissection of the lineage and function of *Gbx2* expressing cells during spinal cord development. *Society for Neuroscience* November 15-19, 2008, Washington DC.
Poster Presentation by B. Luu

22. Reyna SM, **Zervas M** (2008) Molecular and behavioral characterization of mice with a mutation in *Wnt1*. *Society for Neuroscience* November 15-19, 2008, Washington DC.
Poster Presentation by S. Reyna

23. **Zervas M** (2007) Genetic approaches to study cerebellum development, circuitry, and disease. *Tuberous Sclerosis Complex: From Genes to New Therapeutics*. September 23-25.
Poster Presentation by M. Zervas

RESEARCH

Active Funding

1. TS110083 (PI: **Zervas, M**)
DOD-CDMRP Idea Development Award
Dates: 2012-2015

   Temporal loss of Tsc1: Neural development and brain disease in Tuberous Sclerosis

   Role: Principal Investigator; Total Award: $450,000 (direct costs)

   The major goals of this project are to identify critical windows of brain development that are affected by the loss of *Tsc1* and mTOR dysregulation during embryonic development and to ascertain the impact of mTOR inhibition developing neurons during normal development and in Tuberous Sclerosis.

2. P30GM103410 (PI, Attwood, W; COBRE Pilot Sub-award PI: **Zervas, M**)
NIH COBRE award to be used in core facilities to support the work of the Brown Stem Cell Group. Sub-Award: $25,000 (direct costs only)
Dates: April 2012-March 2013

   Determining the dynamic molecular architecture that regulates dopamine neuron diversity

   The major goal of this award is to develop novel genetic tools to evaluate how *Wnt1* and *Lmx1a* converge in progenitors to shape midbrain dopamine neuron diversity *in vivo*.

3. TS100067 (PI: **Zervas, M**)
DOD-CDMRP Exploration Hypothesis Development Award
Dates: 2011-2013

   Determining changes in neural circuits in Tuberous Sclerosis

   Role: Principal Investigator; Total Award: $100,000 (direct costs)

   The major goals of this project are to ascertain how adult thalamocortical circuits and physiology are altered in the absence of *Tsc1* in thalamic neurons.

4. 8P20GM103468-04 (701-1960 sub-award, PI: **Zervas, M**)
   NIH/NCRR/NIGMS
   RI Hospital COBRE Center for Stem Cell Biology
   Competitive Proposal Submission for Full Project
   Dates: 2010-2014 (renewed annually)

   Determining the transcriptional regulation and cell signaling events that shape the molecular identity of dopamine neuron progenitors and specify subtypes of midbrain dopamine neurons

   Role: Principal Investigator; Total Award: $450,000 (direct costs thus far)

   The major goals of this project are to: 1. Elucidate the molecular identity of dopamine neuron progenitors; 2. Determine the genetic basis of dopamine neuron heterogeneity; 3. Investigate the role of WNT, SHH, and FGF8 signaling in establishing the molecular idenity cell and fate specification of dopamine neuron progenitors from embryonic stem cells.

Completed Funding

1. 2-34310 (PI: **Zervas, M**)
   Richard B. Salomon Faculty Research Award
   Date: 2010

   Genetic dissection of midbrain dopamine neuron diversity

   Role: Principal Investigator; Total Award: $15,000 (direct costs only)

   The goal of this project is to identify novel transcriptional regulators of dopamine neuron diversity using mouse genetic mutants, fluorescent activated cell sorting and microarray.

2. 5-27961 (PI, Attwood, W; Sub-award to Zervas, M) COBRE award to be used in core facilities to support the work of the Brown Stem Cell Group. Sub-Award: $12,500 (direct costs only)
   Date: 2011

   Determining the role of mTOR signaling in dopamine neuron cell fate decisions

   The major goal of this award is to develop stem cell based research projects designed to advance our understanding of programming embryonic stem cells and induced pluripotent stem cells. In addition, these funds are intended to foster a multi-disciplinary collaboration in stem cell biology (Brown Stem Cell Group).

3. No Number (PI: Zervas, M)
   NESDB 2011 Meeting Award
   Date: March 25-27, 2011

   Northeast Regional Meeting of the Society for Developmental Biology, Marine Biological Laboratory

   Role: Meeting Organizer and PI; Total Award: $28,000 (direct costs only)

   The award sponsored the 2011 NESDB regional metting, which had the following goals: 1. Promoting a multidisciplinary symposia celebrating novel findings in developmental biology, 2. Expanding graduate student and postdoc interest in developmental biology, 3. Expanding the membership for the Society for Developmental Biology.

4. No number (PI: Zervas, M)
   Brown University Brain Science Program Pilot Research Grant
   Date: 2007

Conditional streptavidin and neuron-specific targeting of biotin conjugates in vivo.

Role: Principal Investigator; Total Award: $15,000 (direct costs only)
The goal of this project was to establish generate a novel transgenic reporter line that expresses both streptavidin and eGFP. The line was established and validated.

5. The Rhode Island Foundation Medical Research Award (PI: Zervas M)
   Dates: 2007

   Genetic neuroanatomy of substantia nigra dopamine neurons

   Role: Principal Investigator; Total Award: $10,000 (direct costs only)
   The goal of this project was to establish a high resolution map of midbrain dopamine neuron subtype distribution in the adult mouse brain. The goals of this project were met.

6. F32HD43533 (PI: Zervas, M)
   NIH Ruth L. Kirschstein National Research Service Award
   Dates: 2003-2006

   Lineage restriction and development of the midbrain and cerebellum

   Role: Principal Investigator, Postdoctoral fellow; Total Award: $150,000 (direct costs)
   The goal of this project was to develop the genetic inducible fate mapping approach to mark and track genetic lineages *in vivo*. The goals of this project were met.

Funding awarded to postdoctoral fellows in the Lab

1. Jeannie Smith, Ph.D., Neuroscience Postdoctoral Fellow
   Brown University Department of Neuroscience Training grant
   Dates: 2012-2013

   The role of Tsc1 in striatal development and in Tuberous Sclerosis

2. Jasmine Yang, Ph.D., Neuroscience Postdoctoral Fellow
   Brown University Department of Neuroscience Training grant
   2008-2009
   Determining age-related changes in dopamine neuron sub-populations and dopamine circuits and establishing a conditional Wnt1 allele to study Wnt1 function in dopamine neurons.

Funding awarded to graduate students in the Lab

1. Brain Science Award
   Dates: September 2012-January 2013
   Integrating Mathematical Modeling and Stem Cell Programming for Neuronal Differentiation
   Awarded to Yu-Ting Liu, graduate student
   Role: Co-Principal Investigator; semester stipend and health fee.

2. Brain Science Graduate Research Award
   Dates: 2009
   Effects of conditionally inactivating Tsc1 in the thalamus during development in a mouse model of Tuberous Sclerosis
   Awarded to Elizabeth Normand, graduate student, September 2009
   Role: Principal Investigator; semester stipend and health fee.

3. Kaplan Summer Graduate Research Award from the Brain Science Institute
   Dates: 2009
   The Contribution of the Wnt1 Lineage to midbrain dopaminergic neurons
   Awarded to Ashly Brown, graduate student, June 2009
   Role: Principal Investigator; Summer stipend.

Funding awarded to undergraduate students in the Lab

1. Brown University UTRA
   Dates: 2009
   *Determining when the ventral tegmental area (VTA) and substantia nigra pars compacta neural circuitry is established from Wnt1-derived dopaminergic neuron***s**
   Awarded to Juliana Guarente undergraduate student, March 03, 2009
   Role: Principal Investigator; Total Award: $3,500.

2. Reismann Fellowship
   Dates: 2008
   Molecular identity, lineage, and genetic neuroimaging of Wnt1 expressing cells
   Awarded to Nellwyn Hagan, graduate student; awarded January 2008
   Role: Principal Investigator; Semester Tuition.

3. Brown University UTRA
   Dates: 2008
   Genetic dissection of the lineage and function of Gbx2-expressing cells during spinal cord development
   Awarded to Brian Luu, undergraduate student, April 01, 2008
   Role: Principal Investigator; Total Award: $3,500.

4. Brown University Galkin Award
   Dates: 2008
   Establishing a 3-dimensional map of dopaminergic neurons
   Awarded to: Sol Reyna, undergraduate student, April 14, 2008
   Role: Principal Investigator; $3,500 (declined).

5. Brown University UTRA
   Dates: 2008
   Determining the role of Wnt1 in midbrain dopamine neurons
   Awarded to Sol Reyna, undergraduate student, April 01, 2008
   Role: Principal Investigator; $3,500 (declined).

6. RI-INBRE Summer Undergraduate Research Fellowship
   Dates: 2008
   Determining the loss of dopamine neurons in mice with a mutation in Wnt1
   Awarded to Sol Reyna, undergraduate student, March 11, 2008
   Role: Principal Investigator; Total Award: $3,500

7. Brown University UTRA
   Dates: 2007
   Defining spinal cord domains by genetic lineage

Awarded to Brian Luu, undergraduate student, March 29, 2007
Role: Principal Investigator: Mark Zervas, Total Award: $3,500

8. Brown University UTRA
   Dates: 2007
   Genetic neuroanatomy of dopamine neurons
   Awarded to Sol Reyna, undergraduate student, March 29, 2007
   Role: Principal Investigator; Total Award: $3,500

Proposals submitted or under review

1. R01 GRANT11145052 (PI: Zervas M)
   NIH R01
   Dates: Apr 01, 2013-March 31, 2018
   The role of Wnt1 in programming embryonic stem cells to become dopamine neurons
   Role: Principal Investigator; Total Award: $1,250,000
   A major goal of this project are to determine how specific concentrations of SHH, FGF8, and WNT1 converge to establish dopamine neuron diversity from embryonic stem cells. An additional goal is to identify the temporal role of *Wnt1* in regulating cell cycle exit and dopamine neuron subtypes using novel conditional embryonic stem cell lines that we developed and that allow for *Wnt1* gene deletion in stem cells at chosen points along the dopamine neuron differentiation pathway.

2. R01 Accession #3425298 (PI: Zervas M)
   NIH-NIMH
   Dates: 2013-2017
   Determining How Tsc1 deletion alters brain development in Tuberous Sclerosis
   Role: Principal Investigator; Total Award: $1,250,000
   The major goals of this project are to identify the mosaic distribution of *Tsc1* mutant cells affects brain development and function and to determine how pharmacological intervention of the *Tsc1*/mTOR pathway with rapamycin affects normal brain development and whether distinct behavioral abnormalities in Tuberous Sclerosis are pharmacologically separable.

3. R01 Accession #3459040 (PI: Zervas M)
   NIH R01
   Dates: Dec 01, 2012-November 30, 2017
   Subcortical brain structures and neurological disease in Tuberous Sclerosis
   Role: Principal Investigator; Total Award: $1,250,000
   The major goals of this project are to conditionally delete *Tsc1* in the striatum during embryonic development and ascertain how FMRP phosphorylation and SAPAP3 protein expression link the mTOR pathway, neural circuits, and repetitive behaviors.

SERVICE

Service to the University

Ph. D. thesis committees (separate from my own students)

2012-Present	Kathryn Coser (MCB Graduate Program)
2011-Present	Alyssa Wheeler (Neuroscience Graduate Program)
2011-Present	Yu-Ting Liu (Program in Biomedical Engineering, MPPB)
2009-Present	Emily Stackpole (Neuroscience Graduate Program)
2009-Present	Diana Donovan (MCB Graduate Program)
2009-Present	Lulu Tsai (MCB Graduate Program)
2008-2012	Atilgan Yilmaz (MCB Graduate Program)
2008-2012	Ed Peckham (MCB Graduate Program)
2009-2011	Eric Lim (MCB Graduate Program)
2008-2010	Martina Strbuncelj **(**MCB Graduate Program)

Academic committees

2009-Present	Institutional Animal Care and Use Committee (IACUC)
2007-Present	Faculty Animal Users Committee
2012	MCB Graduate Students Admission Committee
2011	Faculty Executive Committee
2010	Faculty Executive Committee
2009	Faculty Executive Committee
2008	Curriculum Committee
2008	MCB Graduate Student Annual Retreat Organizer
2007	MCB Graduate Students Admission Committee
2007	Neuroscience Graduate Student Retreat Organizer
2007	MCB Graduate Student Annual Retreat Organizer
2006	Parents weekend Lecture in the program: The New Biology, Disease, Evolution and Education

Additional Service: Transgenic Facility

Gene targeting and homologous recombination are important technical approaches for the mouse genetics community. Many disciplines including immunology, aging, and neurobehavior use the C57Blk6 background as the experimental standard strain of mice. However, commercial stem cell lines of this background have been unreliable and largely unsuccessful for gene targeting. During the last two years, I obtained two C57Blk6 embryonic stem cell lines (graciously provided by Bill Skarnes) and introduced them into our transgenic facility with the goal of gene targeting by homologous recombination in C57Blk6 stem cells. The additional rationale for introducing this resource is that common BAC libraries and current genomic and sequence data are based on mice with C57Blk6 background. In collaboration with the transgenic facility we first validated the karyotype of the stem cell lines. We subsequently targeted the *Wnt1* locus by homologous recombination to generate a conditional *floxed* allele. The targeted stem cells efficiently produced germ line chimeras that were healthy and functional (These findings are presented in a manuscript that is under revision in *Development,* Yang et al., 2012). We subsequently generated a novel

conditional stem cell line that we could delete genes of interest using Cre/loxP technology. The C57Blk6 stem cells are now a common resource being used widely at Brown University.

Service to the profession

2012-Present	K08 Advisory Committee member for Dr. Laura Goldberg M.D., RI Hospital
2006-Present	Reviewer for Development (1-2 per year)
2008-Present	Reviewer for J. Neuroscience (1-2 per year)
2010-Present	Reviewer for PLoS One (2-3 per year)
2011-Present	Reviewer for Nature Neuroscience (1 per year)
2011	Organizer of the Northeast Regional Meeting of the Society for Developmental Biology.
2010	Brain Awareness Week Activities, national event promoted by the Society for Neuroscience. I organized and oversaw a series of activities for fourth grade students including discussing brain anatomy and function, species-specific brain structures and neural networks, Hampden Meadows School, Barrington RI.
2010	Vartan Gregorian Science Conference. I introduced students to the Mexican aquatic salamander, Axolotl, and discussed limb growth and regeneration. My presentation also focused on the putative stem cell population that contributes to the regenerating limb. Vartan Gregorian Elementary School at Fox Point, Providence, RI.
2008	Meetings with Rhode Island Congressional delegation (including Rep. Patrick Kennedy and Sen. Jack Reed) to advocate for stimulus packages funding for NIH funded research at Brown and for universities in RI.

MENTORING

Ph.D. mentoring: Thesis research conducted in the lab

1. Stephen Brown, MCB Ph.D. candidate (June 2007-2011)
   Thesis Project: *Genetic approaches to understand the timing of gene expression and lineage allocation in the mouse auditory system*
   Graduated with Ph.D. May 2011.

2. Nellwyn Hagan, Neuroscience Graduate Student (September 2007-2011)
   Thesis Project: *The Spatial and Temporal Control of Gene Expression in Cerebellum Development*
   Graduated with Ph.D. July 2011.

3. Lindsay Hayes, Brown Neuroscience/NIH Graduate Student Partnership Graduate Student (June 2007-2011)
   *Co-mentor with Dr. Sohyun Ahn, Ph.D.
   Thesis Project: *The role of Shh signaling in dopamine neuron development*
   Graduated with Ph.D. December 2011.

4. Elizabeth Normand, Neuroscience Graduate Student (June 2008-Present)
   Thesis Project: *Determining developmental changes in neural circuits relevant to tuberous sclerosis by conditionally inactivating Tsc1 in the thalamus and cerebral cortex*
   Status: Finishing last year
5. Ashly Brown, Neuroscience Graduate Student (September 2008-Present)
   Thesis Project: *The lineage contribution and functional role of Wnt1 in dopamine neuron development*
   Status: Defense date is December 20, 2012

Postdoctoral mentoring

1. Jeannie Smith, Ph.D., Neuroscience Postdoctoral Fellow
   2012-Present

   Research Project: 1. Determining how the loss of *Tsc1* affects synaptic architecture at thalamocortical synapses; 2. Determining the molecular cascade that links the mTOR pathway to neural circuit formation and synaptogenesis; 3. Conducting mTOR inhibitions studies to determine the time and duration of rapamycin required to ameliorate specific neurologic phenotypes in a novel mouse model that mimics salient features of Tuberous Sclerosis.

2. Jasmine Yang, Ph.D., Neuroscience Postdoctoral Fellow
   2008-2010

   Research Project: 1. Determining the age related changes in dopamine neuron sub-populations and dopamine circuits; 2. Ascertaining whether caloric restriction can ameliorate the effects of aging on dopamine neurons; 3. Identifying the molecular pathogenic cascade underpinning aging dopamine neurons; 4. Generating *Wnt1* conditional allele targeting construct for homologous recombination in mice (completed).

Undergraduate research mentoring

1. Bettina Voelcker, Brown University undergraduate
   BIOL1950/1960, Independent Study
   2012-Present

   Research Project: *Behavioral abnormalities as a result of Tsc1 deletion in the developing thalamus*

2. Catherine Browning, East Providence High School
   Senior Honors Research
   February 2011-2012

   Research Project: Quantitative analysis of behavioral abnormalities mediated by conditional gene deletion of Tsc1 in a mouse model of Tuberous Sclerosis.
   Graduated with senior honors

3. Mariel Rios, Hunter/NYU Neuroscience Research
   BP-ENDURE Program
   June 2011-August 2011

   Research Project: T*he effects of rapamycin treatment on Tsc1 deficient neurons in the thalamus.*

4. Ujla Devyani, UMBC
   MARC U*STAR Summer Intern
   June 2010-August 2010
   Research Project: *Determining the role of Wnt1, Shh, and Fgf8 in the development of midbrain dopamine neurons*

5. Caroline Rieser, Brown University undergraduate student research
   BIOL1950/1960, Independent Study
   February 2009-2010
   Research Project: *Genetic Dissection of Midbrain Dopamine Neuron Diversity*
   Graduated with Senior Honors Thesis

6. Juliana Guarente, Brown University undergraduate student research assistant
   BIOL1950/1960, Independent Study
   February 2009-2010
   Research Project: *Determining the Gbx2 lineage contribution to the adult cerebellum*
   Graduated with Senior Honors Thesis

7. Brian Luu, Brown University undergraduate student research assistant
   BIOL1950/1960, Independent Study
   September 2006-2008
   Research Project: *Elucidating the role of Gbx2 in spinal cord development*
   Graduated with Senior Honors Thesis

8. Sol Reyna, Brown University undergraduate student research assistant
   BIOL1950/1960, Independent Study
   September 2006-2008
   Research Project: *Establishing a 3-D quantitative map of dopamine neurons in the adult midbrain and behavioral analysis of mutant mice with dopamine neuron loss*

TEACHING

1. BIOL1310/2310 Analysis of Development
   Spring semester, 2012
   Course Leader and Sole Instructor
   Enrollment: 18 (2 Graduate students, 16 Undergraduates)
   Course Evaluation: 1.45 (out of 5: 1 = excellent; 2= very good)
   Instructor Evaluation: 1.20 (out of 5: 1 = excellent; 2= very good)

2. BIOL1310/2310 Analysis of Development
   Spring semester, 2011
   Co-Instructor
   Enrollment: 12 (2 Graduate students, 8 Undergraduates)
   Course Evaluation: 1.42 (out of 5: 1 = excellent; 2= very good)
   Instructor Evaluation: 1.08 (out of 5: 1 = excellent; 2= very good)

3. BIOL2320A Current Topics in Developmental Biology: Cell Fate and Lineage Decisions in Neural Development and neurological diseases

Fall semester, 2010
Course Leader and Instructor

Enrollment: 6 (3 Graduate students, 3 Undergraduates)
Course Evaluation: 1.40 (out of 5: 1 = excellent; 2= very good)
Instructor Evaluation: 1.20 (out of 5: 1 = excellent; 2= very good)

4. BIOL1310/2310 Analysis of Development
Spring semester, 2010
Course Leader and Instructor

Enrollment: 12 (2 Graduate students, 10 Undergraduates)
Course Evaluation: 1.40 (out of 5: 1 = excellent; 2= very good)
Instructor Evaluation: 1.10 (out of 5: 1 = excellent; 2= very good)

5. BIOL1310/2310 Analysis of Development
Spring semester, 2009

Enrollment: 14 (2 Graduate students, 12 Undergraduates)
Course Evaluation: 1.44 (out of 5: 1 = excellent; 2= very good)
Instructor Evaluation: 2.11 (out of 5: 1 = excellent; 2= very good)

6. BIOL2320 Topics in Developmental Biology: Genetic Control of Cell Fate Decisions
Fall semester, 2008
Co-Instructor

Enrollment: 3 Undergraduates (2 received grades; 1 received no credit)
Course Evaluation: 1.0 (out of 5: 1 = excellent; 2= very good)
Instructor Evaluation: 1.0 (out of 5: 1 = excellent; 2= very good)

7. BIOL1310/2310 Analysis of Development
Spring semester, 2008
Instructor

Enrollment: 29 (8 Graduate students, 21 Undergraduates)
Course Evaluation: 2.12 (out of 5: 1 = excellent; 2= very good)
Instructor Evaluation: 2.19 (out of 5: 1 = excellent; 2= very good)

8. BIOL1310
March 20, 2007
Guest Lecturer: *Regionalization of the neural tube*

9. BIOL110
March 7, 2007
Guest Lecturer: Development, Physiology, and Pathology of Midbrain Dopamine Neurons