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Curriculum Vitae

Kirill Zavalin

Postdoctoral Fellow

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Education

2013-2022 **Vanderbilt University**, Nashville, TN, **PhD in Neuroscience**
Advisors: Dr. Andre H Lagrange, Dr. Eric Delpire
Thesis: "Two Tales of Cortical GABAergic System Development"

2006-2010 **Duke University**, Durham, NC, **BS in Biology**, Russian studies minor

Current Research

Since joining the research group of Dr. Jingqiong Kang in July of 2022, I am investigating neuronal pathophysiology of genetic epilepsy disorders associated with mutant variants of GAT-1 and $GABA_AR$ subunits, namely β3 subunit. I investigate how these mutant variants affect GABAergic neurotransmission and GABA uptake in *ex vivo* living neurons by techniques including electrophysiology, and pathologic expression of GABAergic system components by immunohistochemistry. I have identified several important pathologies in mice expressing GAT-1(S295L) and $GABA_AR$ β3(N328D), such as altered GABA uptake and changes in GABAergic synaptic neurotransmission. I presented my findings at American Epilepsy Society and *SLC6A1* symposium in 2022, and will present at AES again in December 2023.

Dissertation Research

My dissertation research focused on progressive changes in subunit composition of γ-Aminobutyric acid (GABA) type A receptors ($GABA_ARs$) and late expression of potassium-chloride transporter KCC2 that alter GABAergic signals during development to fit unique developmental functions.

KCC2 and Cortical Development of Interneurons

I conceived the project to investigate the role of KCC2 in development of cortical GABAergic interneurons by use of conditional knockout mice, employing *ex vivo* electrophysiology and immunohistochemistry/microscopy of mouse brain sections. I found that while some interneurons express KCC2 earliest among cortical neurons, loss of KCC2 does not impact interneuron migration contrary to models in the field. However, my research has shown that KCC2 is crucial to normal function of interneurons, with the knockout resulting in early death, failure to thrive, and seizures in mice. I found changes in distribution of interneurons that occur later during development, notably affecting parvalbumin+ interneurons, that may underlie this phenotype.

Developmental Changes in $GABA_AR$ Subunit and KCC2 Expression

I and co-authors undertook a comprehensive investigation of progressive changes in $GABA_AR$ subunit and KCC2 expression throughout cortical development using Western blot and immunohistochemistry techniques. We characterized expression patterns that corroborate previously published data, but offer considerably greater resolution of temporal and layer-specific changes in expression that expand our understanding of GABAergic system development and will be useful for future targeted studies in the field.

Research Positions

2022- Postdoctoral Fellow, laboratory of Dr. Jingqiong Kang, Vanderbilt University Medical Center

2013- 2014 Interdisciplinary Graduate Program in Biomedical Sciences, Vanderbilt University

2007-2013 Student Intern/Research Assistant in Laboratory of Dr. Ela Knapik, Vanderbilt University
Studied ER-to-Golgi trafficking machinery using genetic tools in zebrafish

Presentations and Awards:

Oral Presentations

2022 ***SLC6A1* Symposium at American Epilepsy Society Meeting**
"The GABAergic System and the Role of GAT-1"

2021, 2019 **Lake Cumberland Biological Transport Meeting**
"Excitatory to Inhibitory Transition in GABAergic Currents Guides Circuit Formation of Cortical Interneurons"
Best Presentation Award (2021)

2021-2016 **Vanderbilt University Nano-Symposium**
Annually Presented on Topics Regarding K-Cl Transporter 2 in Interneuron Development and $GABA_A$ Receptor Isoform expression during Cortical Development

2018 **Kennedy Center Science Day**
"Excitatory to Inhibitory Transition in GABAergic Currents Guides Circuit Formation of Cortical Interneurons"

Poster Presentations

2023 **American Epilepsy Society Annual Meeting**
"Reduced GABA Uptake and Altered GABAergic Neurotransmission in Slc6a1S295L Knock-In Mouse Associated with Epileptic Encephalopathy"
Selected for Poster Highlights Session (2023)

2022 **American Epilepsy Society Annual Meeting (2 posters)**
"Region and Layer-specific Expression of Functionally Distinct GABAA Receptor Isoforms and KCC2 in Developing Cortex"

"GABA Uptake, Tonic GABAergic Current, and GABA Levels in the *Slc6a1*$^{+/A288V}$ and *Slc6a1*$^{+/S295L}$ Mouse Models of Developmental and Epileptic Encephalopathy"

2021, 2020, 2018 **American Epilepsy Society Annual Meeting**
"Excitatory to Inhibitory Transition in GABAergic Currents Guides Circuit Formation of Cortical Interneurons"
Young Investigator Award (2020)

2021 **Society for Neuroscience Global Connectome**
"Excitatory to Inhibitory Transition in GABAergic Currents Guides Circuit Formation of Cortical Interneurons"

2019, 2018 **Kennedy Center Science Day**
"Excitatory to Inhibitory Transition in GABAergic Currents Guides Circuit Formation of Cortical Interneurons"
Graduate Student Poster Award (2018)

2019 **Society for Neuroscience Meeting**
"Excitatory to Inhibitory Transition in GABAergic Currents Guides Circuit Formation of Cortical Interneurons"

2019 **Vanderbilt Department of Anesthesiology Retreat**
"Excitatory to Inhibitory Transition in GABAergic Currents Guides Circuit Formation of Cortical Interneurons"

2018 **Tennessee Physiological Society 2018 Annual Meeting**
"Excitatory to Inhibitory Transition in GABAergic Currents Guides Circuit Formation of Cortical Interneurons"

2022, 2018-, 2015 **Vanderbilt University Neuroscience Retreat**
"Annually Presented on Topics Regarding K-Cl Transporter 2 in Interneuron Development and $GABA_A$ Receptor Isoform expression during Cortical Development

2013, 2012 **Vanderbilt University Annual Cell and Developmental Biology Retreat**
"Paralog-Specific Function of Sec23a and Sec23b in Cartilage Morphogenesis"

2012 **Vanderbilt University Developmental Biology Retreat**
"Paralog-Specific Function of Sec23a and Sec23b in Cartilage Morphogenesis"
Research Assistant Poster Presentation Award

Other Awards

2023 American Epilepsy Society Fellow

2023 Vanderbilt Postdoctoral Training Program in Functional Neurogenomics

2014 Vanderbilt Graduate Neuroscience Program Training Grant

Conferences Attended

2021, 2019 Society for Neuroscience Meeting

2022, 2021, 2020, 2018 American Epilepsy Society Meeting

Publications

Zavalin, K., Hassan, A., Fu, C., Delpire, E., and Lagrange, A.H. (2022). Loss of KCC2 in GABAergic Neurons Causes Seizures and an Imbalance of Cortical Interneurons. *Frontiers in Molecular Neuroscience* 15. doi: 10.3389/fnmol.2022.826427.

Zavalin, K. and Hassan, A. (co-authors), Lagrange, A.H. "GABAA Receptor Expression in Developing Cortex" (In preparation)

Li, W., Chen, L., Fleming, J.T., Brignola, E., **Zavalin, K.**, Lagrange, A., Rex, T., Heiney, S.A., Wojaczynski, G.J., Medina, J.F., et al. (2022). Dendritic Inhibition by Shh Signaling-Dependent Stellate Cell Pool Is Critical for Motor Learning. Journal of Neuroscience *42*, 5130–5143. 10.1523/jneurosci.2073-21.2022.

Nwosu GI, Shen W, **Zavalin K**, Poliquin S, Randhave K, Flamm C, Biven M, Langer K, Kang JQ. GABAA Receptor β3 Subunit Mutation N328D Heterozygous Knock-in Mice Have Lennox-Gastaut Syndrome. Int J Mol Sci. 2023 May 8;24(9):8458. doi: 10.3390/ijms24098458. PMID: 37176165; PMCID: PMC10179596.

Professional Skills:

- Mouse and rat brain dissection (including neonatal timepoints) and preparation for *ex vivo* electrophysiological recordings, histochemistry, and Western blot analysis
- *In vitro* and *ex vivo* electrophysiology
- Immunohistochemical and Western blot analysis of mouse brain, focusing subtype markers of GABAergic cortical neurons, $GABA_A$ receptor subunits, and KCC2
- Familiarity with multiple GABAergic neuron lineage mouse lines like Dlx5, parvalbumin, and Nkx2.1 to create fluorescent reporter lines or conditional deletion
- Common molecular biology techniques
- Extensive experience in epifluorescent and confocal microscopy, including managing use and technical troubleshooting of a confocal microscope and an epifluorescent microscope
- Mouse husbandry and colony maintenance
- Proficiency with Python, ImageJ, Adobe Illustrator, Adobe Photoshop, MS Office, Graphpad Prism, Leica LAS X microscope imaging software

Professional Activities:

2023-2018	Training undergraduate interns, mentoring graduate students Megan Alder, Undergraduate Student, 2018-2019 Wen Li, Postdoctoral Fellow, 2020 (provided training in electrophysiology) Katherine Langer, Undergraduate Student, 2022-2023 Rishi Pillai, Undergraduate Student, 2022-2023 Gerald Nwosu, Graduate Student, 2023 Melissa DeLeeuw, Graduate Student, 2022-2023
2022-2018	Basic training of graduate students, postdocs, and other staff in microscopy and electrophysiology techniques
2019-2015	Osher lecture for senior citizens, “Brain Inhibition: Function, Disorders, and Therapeutic Targeting”
2019-2015	Brain Blast (educational community outreach by Vanderbilt Brain Institute) Participated annually, organized a presentation booth (2019)
2019	NURO345 Fundamentals of Neuroscience (graduate level) teaching assistant