DOI: 10.46991/JISEES.2025.SI1.181

Bridging *In Vitro* Electrophysiology and *In Vivo* Behavior in Zebrafish Models of Autism Spectrum Disorder

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ABSTRACT

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by challenges in social interaction, communication, and the presence of restricted and repetitive behaviors. While the neurobiological underpinnings of ASD remain elusive, understanding the function of individual neurons and their integration into circuits is critical. The zebrafish (*Danio rerio*) offers a powerful model system for dissecting neural circuit function due to its genetic tractability, external development, larval transparency, and conserved neuroanatomy. This presentation highlights the utility of the zebrafish model for investigating ASD-relevant neural circuitry through a combined *in vitro* and *in vivo* approach. We focus on isolating specific neuronal populations from zebrafish models of ASD to perform *in vitro* electrophysiological recordings, characterizing their intrinsic electrical properties and synaptic signaling deficits at the single-cell level. These *in vitro* findings regarding altered neuronal excitability and connectivity are then validated *in vivo* by assessing corresponding behavioral phenotypes in intact zebrafish larvae using established paradigms for social interaction, locomotion, and sensory processing. By correlating cellular-level electrical dysfunction observed *in vitro* with circuit-level activity and complex behaviors *in vivo*, we aim to bridge the gap between molecular/cellular deficits and the emergent behavioral characteristics of ASD. This integrated approach using the zebrafish model provides a valuable platform for identifying specific neuronal contributions to ASD pathophysiology and offers potential avenues for high-throughput screening of therapeutic interventions targeting neuronal function. The insights gained from these studies contribute to a more comprehensive understanding of ASD neurobiology and facilitate the translation of findings towards clinical applications.

Keywords: Autism Spectrum Disorder, zebrafish model, electrophysiology, neuronal excitability

References:

1. Zhuang, H.; Liang, Z.; Ma, G.; Qureshi, A.; Ran, X.; Feng, C.; Liu, X.; Yan, X.; Shen, L. Autism spectrum disorder: pathogenesis, biomarker, and intervention therapy. *MedComm,* **2020**, *5*, e497. DOI:10.1002/mco2.497
2. Vaz R., Hofmeister W., Lindstrand A. Zebrafish models of neurodevelopmental disorders: limitations and benefits of current tools and techniques. *Int. J. Mol. Sci.* **2019**, *20*,1296. DOI:10.3390/ijms20061296

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