sense a wide range of extracellular guidance cues. The pharmacological elimination of growth cone filopodia results in axon guidance defects without impeding axon elongation; however, the molecular and cellular mechanisms that regulate growth cone filopodia dynamics remain unknown. Fascin1 is a ~55 kDa actin bundling protein that crosslinks actin filaments to form tight F-actin bundles in filopodia and is a known regulator of cell migration. Fascin1 is highly expressed in developing neurons and enriched in growth cone filopodia, but its role in growth cone motility and guidance has not been investigated. Here, we use a combination of cell culture and *in vivo* approaches to investigate the role of fascin1 in axon development. We have developed a CRISPR-Cas9-mediated approach to knock out fascin1 in primary neurons to allow us to examine filopodial dynamics, axon extension/branching, and guidance response. In addition, we demonstrate how the loss of Singed, the *Drosophila melanogaster* ortholog of fascin1, affects *in vivo* brain wiring and function. We found that *singed* null flies exhibit marked axonal defects in the mushroom body, a center for learning and memory. We have also discovered phototaxis defects in *singed* null flies that we speculate are due to circuitry errors. Together, our work highlights the important role of Fascin1 in actin-based axon development and brain wiring. Additionally, the use of both a cultured cell system and an *in vivo* model allows us to examine the neurodevelopmental function of Fascin1 at both the single cell and organismal levels.

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Topic: AS01 Nervous System Development and Related Disorders

MICE LACKING A NOVEL PHOSPHOSITE S1014 ON THE MET RECEPTOR TYROSINE KINASE DISPLAY ASD-ASSOCIATED BEHAVIORAL PATTERN

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Receptor tyrosine kinase MET is an oncogene involved in multiple cellular functions. Within a phosphoproteomics study, we identified previously unreported phosphorylation on serine 1016 (mouse S1014) of MET. Knock-in mice lacking the phosphorylation on S1014 (S1014A) showed a stereotypical, circling movement pattern, a plausible sign of autistic behavior. As variants of the MET gene are enriched in patients with autism spectrum disorder (ASD), we aimed to study the impact of MET S1014 on neurodevelopment. We employed a behavioral battery (n = 12) targeting anxiety and locomotor activity, social domain, repetitive behavior, and cognition. We quantified neuronal density and the number of GABAergic inhibitory PV- and SOM-expressing interneurons in brain regions of interest at different stages of mouse development. In a tube test, S1014A homozygous mice of both sexes demonstrated a significantly higher level of social dominance over their WT mates (S1014A = 71% vs WT = 29%, $p \leq 0.05$). This finding correlated with reduced anxiety of S1014A mice observed in the "open field" and with a higher number of aggressive attacks in the "reciprocal social interaction" tasks. Additionally, we have detected a significant increase in the number of parvalbumin-expressing interneurons in the striatum (S1014A = 109.4 ± 31.8 vs WT = 30.2 ± 14.1, $p \leq 0.05$), which is consistent with the data pertaining to known MET knock-out models. Lack of MET S1014 phosphorylation impacts social behavior and alters the expression of inhibitory PV interneurons. We are currently exploring the underlying molecular mechanisms of these phenomena by analyzing the data (n = 5) from single-nuclei RNA sequencing of the prefrontal cortex (PFC), which is responsible for the dominant behavior of the mice. In addition, we are targeting 12 mRNA probes with HiPlex RNAscope in PFC, striatum, and lateral septum to explore the possible disbalance of excitation and inhibition, one of the core mechanisms of ASD development.

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Topic: AS01 Nervous System Development and Related Disorders

H-ABC MURINE MODEL PRESENTS ASTROGLIOSIS AND REACTIVE ADULT NEUROGENESIS

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H-ABC is a neurodegenerative disease caused by mutations in TUBB4A, characterized by hypomyelination and brain malformations. Clinically, it shows motor development delay, pyramidal and extrapyramidal movements, ataxia, spasticity, and cognitive and sensory deficits. Under physiological conditions, neural stem cells (NSCs) of the adult brain's subventricular zone (SVZ) can generate new neurons and oligodendrocytes capable of migration. Neurogenic activity has also been observed after some pathological processes. *Taiep* rat carries a mutation in TUBB4A, representing an excellent model for studying this disease and the neurogenic response to the neurodegenerative process. To detect cell proliferation in the SVZ, we injected *taiep* rats and WT control animals with Bromodeoxyuridine. After 12 hours, animals were transcardially perfused, the brain removed, and processed for fluorescence immunohistochemistry. We used antibodies against BrdU, GFAP, PLP, neurofilaments, and myelin. We found hyperplasia of the SVZ in the H-ABC model observed as a thicker band of proliferative cells in the neurogenic region. In addition, the corpus callosum and cerebellum in *taiep* showed severe demyelination, confirming previous results. In these regions, there is also astrocytosis, which could indicate a reaction to the degenerative process and a high rate of proliferative cells to the astroglial line. We propose two possible hypotheses for these changes, i.e., some of the regulatory signaling pathways involved in the neurogenic processes could be disrupted in TUBB4A-expressing cells. Alternatively, the tubulin mutation blocks the ability of new cells to migrate to their destination, inducing an accumulation of cells in the neurogenic region of the SVZ. We conclude that H-ABC