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Research Week

Astrocytic Mechanisms of Developmental Synapse Elimination in Drosophila

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Neuronal remodeling is a crucial step towards healthy maturation of synapses, circuits and eventually brain function This process involves changes in neuron morphology such as pruning of dendrites, axons, or synapses, which is mediated in part by non-neuronal cells called glia. While glia are known to be required for this process, we still have not defined how glia appropriately identify and eliminate only those synapses or neurites that require pruning. Given that many neurodevelopmental and neurodegenerative disorders such as autism spectrum disorder (ASD) and Alzheimer's Disease (AD) involve a major loss of synapses, and some glial pruning mechanisms appear to be inappropriately re-activated during disease, elucidating how glia accomplish these tasks will be crucial to finding therapeutic targets to prevent or reverse this loss. Drosophila offers a great model to study neuronal remodeling and the glia-neuron interactions involved as they have both neurons and astrocytes, they undergo a period of synapse elimination in early adulthood comparable to the developing mammalian brain and have many genetic targeting and imaging tools. We performed a genetic screen for novel glial regulators of synapse elimination in Drosophila and found Croquemort (Crq), a scavenger receptor with roles in the immune system for engulfment of apoptotic cells. Thus, we sought to investigate which neuronal populations utilize astrocyte Crq to prune their synapses and to elucidate the mechanisms by which Crq mediates this process. We used high-resolution imaging and protein assay techniques to investigate which neuronal populations undergo developmental synapse elimination and how this is affected by crq knockdown. Preliminary data shows us that cholinergic and glutamatergic neurons undergo synapse elimination during development while GABAergic neurons do not. Further work will aim to determine whether these neuronal subtypes require Crq to prune their synapses and how neural activity affects Crq's function.