Uncovering the transcriptional landscape of astrocytes highlights glial Actin dynamics as important for neuronal remodeling

Neta Marmor-Kollet[1], Victoria Berkun[1], Hadas Keren-Shaul[2], Ido Amit[3] & Oren Schuldiner[1]

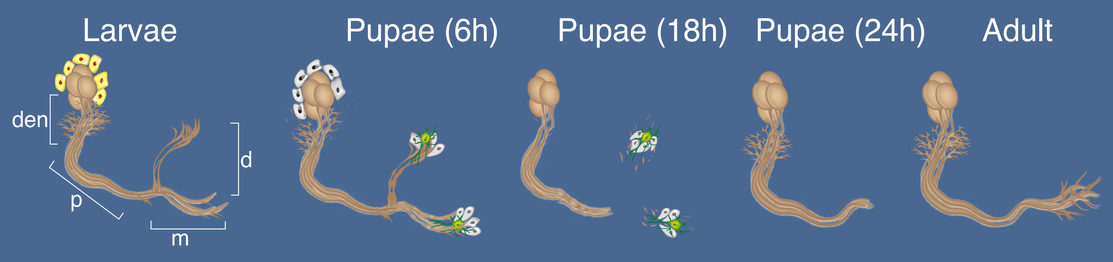
[1]Weizmann Institute of Science, Dept. of Molecular Cell Biology, [2]Weizmann Institute of Science, Life Sciences Core Facilities, [3]Weizmann Institute of Science, Dept of Immunology, Rehovot, Israel.

Introduction

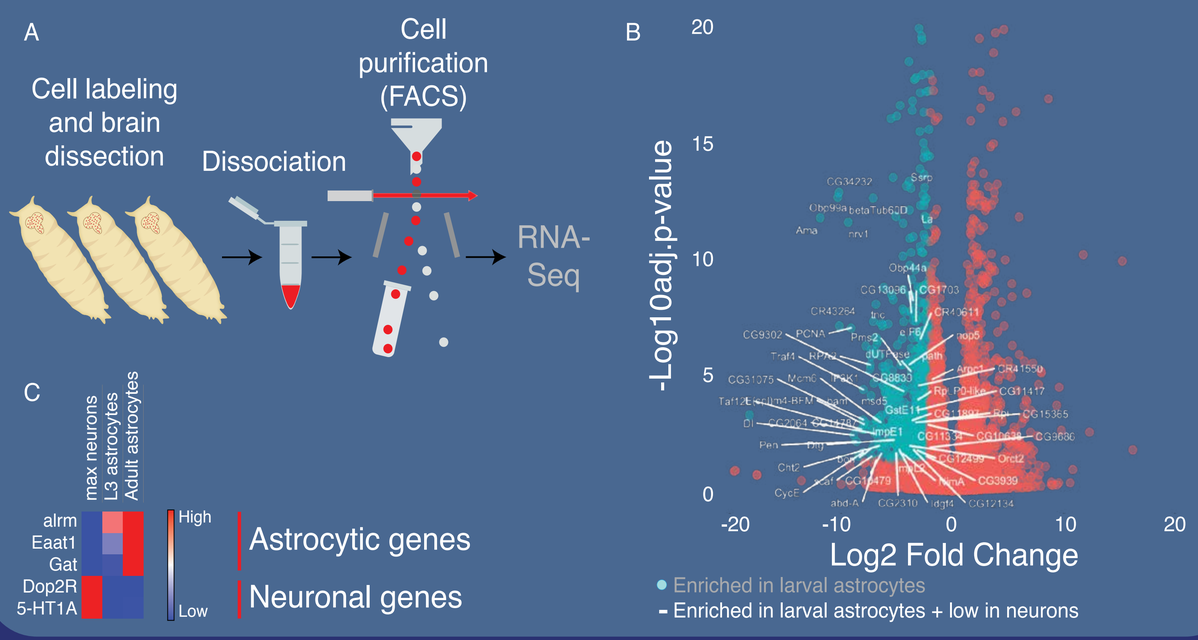
• Developmental neuronal remodeling is an evolutionary conserved mechanism used to sculpt the mature nervous system. It often involves pruning of exuberant connections as a mechanism to refine neural circuits.

• Developmental axon pruning of *Drosophila* mushroom body (MB) γ neurons is a unique model to to study glia-neuron interactions during pruning due to its stereotypic occurrence, and the genetic tools available.

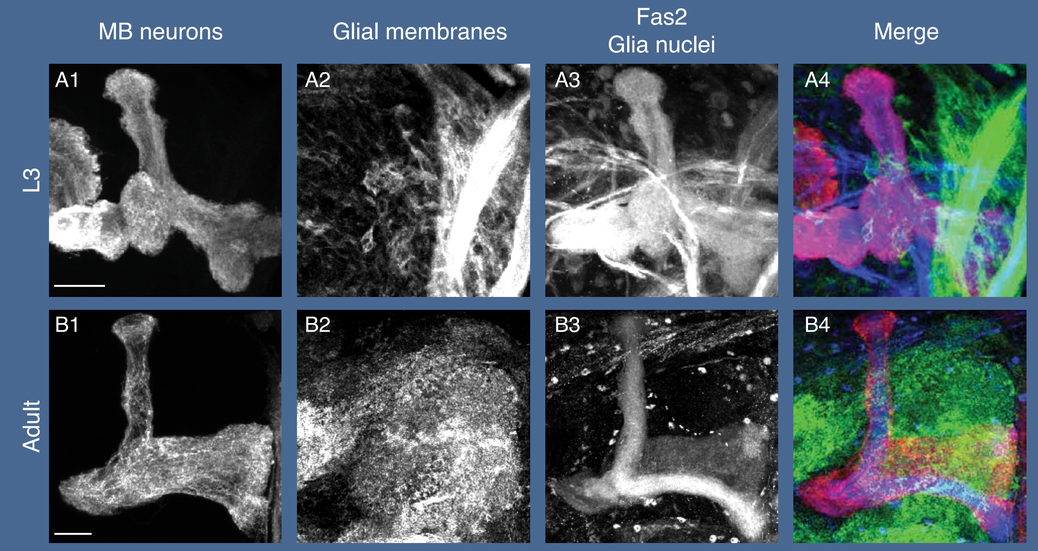
• Astrocytes have been found to play key roles in the clearance of axonal debris but whether they have additional roles, as well as the full extent of these glia-neuron interactions during remodeling, remains unknown.



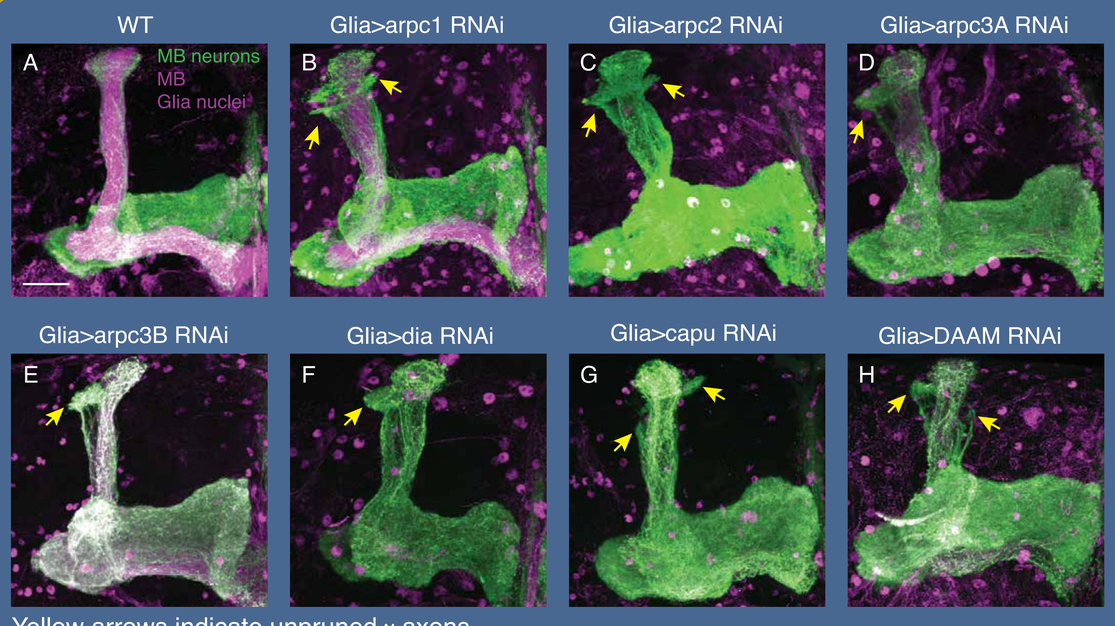
A Expression profiling of astrocytes reveals a dramatic developmental program



B Dual binary expression systems enable labeling and manipulation of both glia and neurons simultaneously

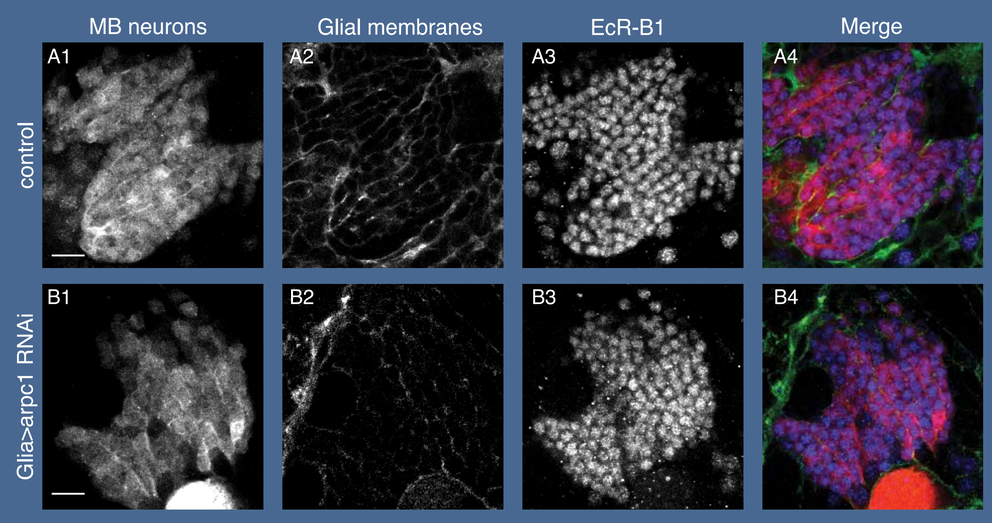


C Glial F-actin is necessary for MB γ-axon pruning

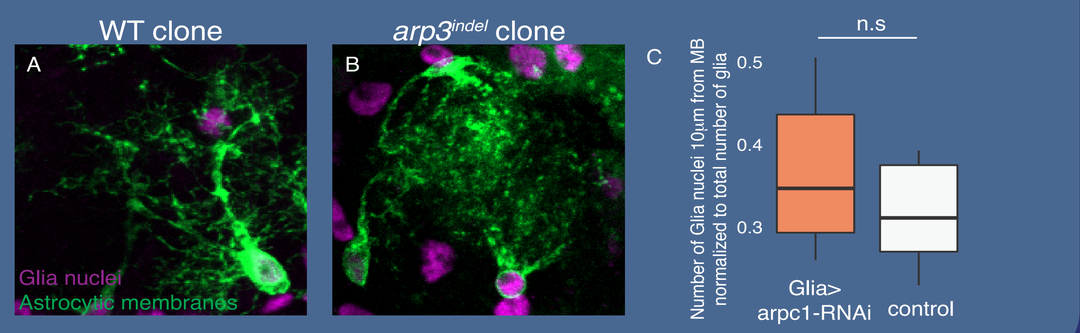


Yellow arrows indicate unpruned γ axons.

D Glial Arpc1 is not required for neuronal expression of EcR-B1



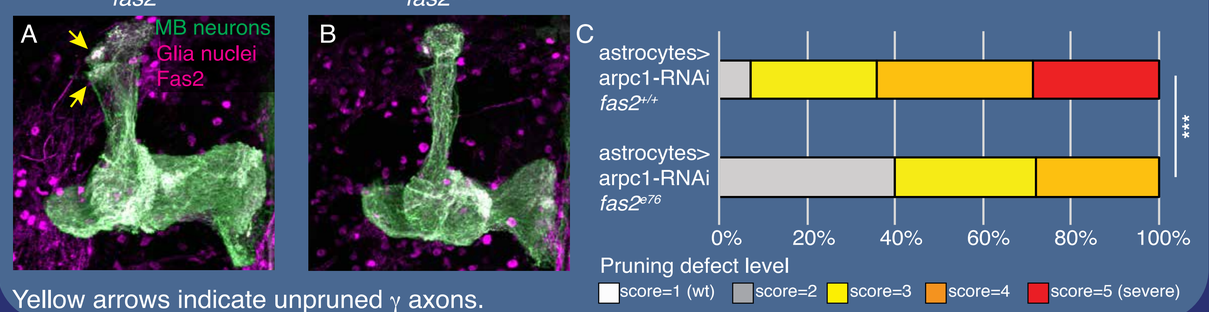
E Disturbing glial F-actin does not cause gross changes in migration or morphology of astrocytes



F Astrocytic F-actin is required for their infiltration of the axonal bundle at the onset of pruning

The MB dorsal lobe is marked with a white line.
Yellow arrows indicate astrocytic membranes inside the dorsal lobe.

G Decreasing axonal adhesion suppresses astrocytic Arpc1-induced pruning defect



Yellow arrows indicate unpruned γ axons.

Summary

• F-actin regulating genes are differentially expressed during the development of astrocytes.

• Knocking down F-actin regulating genes in glia results in MB γ axon pruning.

• Knocking down Arpc1 in astrocytes prevents their ability to infiltrate the axonal bundle at the onset of pruning.

• Decreasing MB axonal adhesion suppresses astrocytic Arpc1-induced pruning defect.