Similarities in fruit fly nervous systems transform view of metamorphosis

March 15 2016

Drosophila sp fly. Credit: Muhammad Mahdi Karim / Wikipedia. GNU Free Documentation License, Version 1.2

New research from the Howard Hughes Medical Institute transforms the current view that metamorphosis in fruit flies, whereby larvae change into adults, consists of two separate stages.

The study, to be published in the journal *eLife*, shows that while larval and adult *Drosophila* fruit flies have strikingly different nervous systems to support their different body structures and needs, their systems are made of neurons with similar structures and molecular signatures. This suggests that *Drosophila* neural stem cells changed minimally during the fly's evolution from its ancestors, which did not undergo metamorphosis.

Adult and larval fruit fly nervous systems develop from the same set of stem cells known as neuroblasts. These neuroblasts undergo two separate phases of proliferation where they generate multiple neurons. The first phase occurs in the embryo to create neurons of the larval nervous system, and the second occurs in the larva to create neurons of the adult nervous system.

These phases are separated by a brief period where no proliferation occurs. The similarity between adult and larval neurons is due to the internal state of the neuroblasts remaining similar before and after the period of inactivity.

"The two-phase pattern seems to change the idea of metamorphosis as two separate stages," says first author Haluk Lacin.

"It evolved from a simpler scheme, such as seen in grasshoppers, whereby all neurons were generated during an extended embryonic phase."

The team used a lineage tracing method to establish a link between neurons in the adult and larval nerve cords, which are equivalent to the human spinal cord.

The method involved visually screening publicly available databases to identify over 100 lines of the protein GAL4, which has an expression restricted to one or a few embryonic neuroblasts. To highlight which neuroblast lineages are marked by these GAL4 lines, they generated random lineage clones for each and compared their structure and molecular expression to previously published embryonic neuronal lineages.

"Our findings showed that the neurons arising from the two distinct phases of neuroblast proliferation express similar molecular markers and extend similar nerve fibers, although they function in two very different nervous systems," Lacin explains.

"Neuroblasts in non-metamorphosing insects multiply continuously. We therefore believe that, during the evolution of metamorphosis, a break was inserted into the continuous proliferation of neuroblasts in non-metamorphosing insects, without a significant impact on the neuronal types generated."

During the study, the researchers also discovered three neuroblasts that appear to be unique to the middle, or thoracic, segments of *Drosophila*. The presence of these neuroblasts depends on genes that control positional information during the development of animal body plans.

"Two of these neuroblasts generate leg motor neurons. Since flies have legs only in thoracic segments, the presence of neuroblasts in these segments indicates the coordination of neurogenesis with development of the body plan at the stem-cell level," says James Truman, co-author of the study.

"The third neuroblast is novel and appears to have arisen recently during insect evolution. Based on anatomy and molecular markers, we propose that it arose by duplication of a neighboring stem cell, which may have enabled finer neuronal control over leg-related behaviors, such as walking and grooming."

The nerve cord in *Drosophila* has been used as a model system for over

30 years to understand how neuroblasts generate a highly complex but organized tissue. Lacin and Truman believe the insights from their study will now make it possible to investigate how molecular events, which occur from embryonic to adult stages, control the formation and function of the nervous system in fruit flies, with possible translation to humans.

More information: Haluk Lacin et al. Lineage mapping identifies molecular and architectural similarities between the larval and adult central nervous system , *eLife* (2016). DOI: 10.7554/eLife.13399

Provided by eLife