Researchers discover Chinmo, 'the youth gene'

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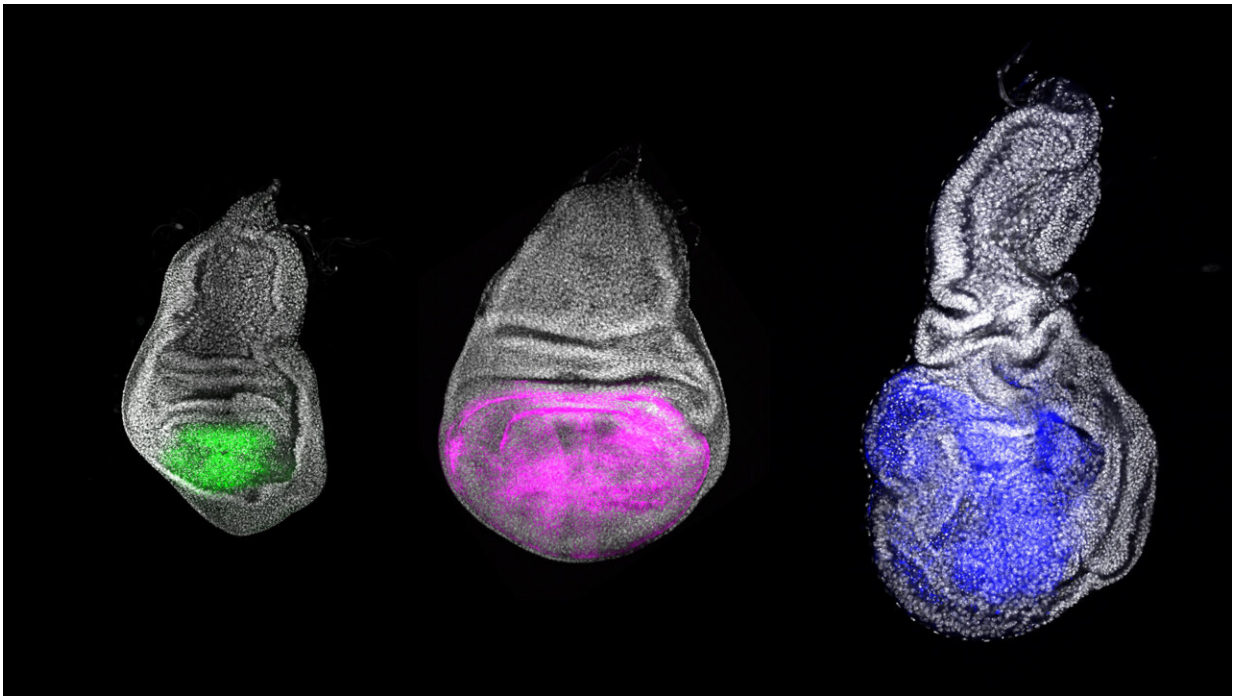

Absence of Chinmo in imaginal cells suppresses wing growth (left) compared to control wing precursor tissue (middle), while overexpression of the Chinmo gene induces tissue overgrowth, as occurs in processes tumors (right). Credit: IBE

A new study published on *eLife* and led by the Institute for Evolutionary Biology (IBE, CSIC-UPF) and the IRB Barcelona, has revealed that the Chinmo gene is responsible for establishing the juvenile stage in insects. It also confirms that the Br-C and E93 genes play a regulatory role in

insect maturity. These genes, which are also present in humans, act as a promoter and as a suppressor, respectively, of cancerous processes.

The results of the research, which was carried out with the fruit fly Drosophila melanogaster and the cockroach Blatella germanica, reveal that these genes have been conserved throughout the evolution of insects. Therefore, it is believed that they could play a key role in the evolution of metamorphosis.

The Chinmo, Br-C, and E93 genes are the hands of the biological clock in insects

Insects that undergo complete metamorphosis, such as flies, go through the following three stages of development: the embryo, which is formed inside the egg; the larva (juvenile stage), which grows in several phases; and the pupa, which is the stage that encompasses metamorphosis and the formation of the adult organism.

Previous studies had discovered that the Br-C gene determines pupal formation in insects. In 2019, the same IBE team that has led this study described the essential function of E93 to complete metamorphosis in insects and initiate the maturation of the tissues that go on to form the adult. However, the gene responsible for determining the juvenile stage was unknown until now. This study has now identified the Chimno gene as the main precursor of this stage in insects.

By deleting the Chinmo gene in Drosophila specimens, the scientists observed that these insects progressed to the pupal stage without completing the juvenile stage, moving to the adult stage early. These findings thus confirm that Chinmo is essential for juvenile development.

"We have discovered that Chinmo promotes tissue growth during the

juvenile stage of Drosophila by keeping the cells undifferentiated. Thus, while Chinmo is expressed, cells cannot differentiate as the gene suppresses the action of those genes responsible for forming adult tissues," says Dr. Xavier Franch, a researcher at the IBE (CSIC-UPF) who co-led the study.

Thus, the study concludes that the Chinmo gene has to be inactivated for Drosophila to progress from the juvenile to the pupal stage and to carry out metamorphosis successfully. Likewise, it confirms that the sequential action of the three genes, namely Chinmo, Br-C, and E93, during the larval, pupal, and adult stages, respectively, coordinate the formation of the different organs that form the adult organism.

Growth-regulating genes play a key role in cancerous processes

Chinmo and Br-C belong to the large family of BTB-ZF transcription factors—proteins involved in cancer and that are also found in humans. Although previous studies had shown that Chinmo is a precursor of cancer, the role of Br-C and E93 in this disease was unknown until now.

"Understanding the molecular functioning of cell growth can help to better comprehend cancer processes. Healthy cells grow, differentiate, and mature. In contrast, cancer cells grow uncontrollably, do not differentiate, and fail to mature. So determining the role of Chinmo, Br-C, and E93 may be key to future clinical research," says Dr. Jordi Casanova, an IRB Barcelona researcher and co-author of the study.

The study shows that while Chinmo is an oncogenic precursor because it promotes tissue growth and prevents differentiation, C-Br and E93 serve as tumor suppressors by activating tissue maturation.

Chinmo reveals how metamorphosis evolved

The complete metamorphosis of insects such as butterflies and flies is an evolutionary innovation that has emerged gradually during the evolution from insects that undergo a much simpler metamorphosis, such as cockroaches. To understand how this gradual process has taken place, the researchers analyzed the function of Chinmo, Br-C, and E93 in cockroaches.

"Analyzing the function of these genes in different species of insects allows us to observe how evolution works. The observation that Chinmo function is conserved in insects as evolutionarily separated as flies and cockroaches gives us clues as to how metamorphoses originated," explains Dr. David Martin, a researcher at the IBE (CSIC-UPF) who co-led the study.

The results of the study indicate that the regulatory action of Chinmo and E93 in more basal insects such as the cockroach are sufficient to determine the transition from the juvenile to the adult form. However, the introduction of the Br-C gene allowed the development of the pupae and the appearance of complete metamorphosis through a new pupal stage in insects such as flies.

More information: Sílvia Chafino et al, Antagonistic role of the BTB-zinc finger transcription factors chinmo and broad-complex in the juvenile/pupal transition and in growth control, *eLife* (2023). DOI: 10.7554/eLife.84648

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