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CALYPSO, A PcG GENE, REGULATES THE DEVELOPMENT OF TUMOR-LIKE MALFORMATION OF EYES VIA INSULIN SIGNALING PATHWAY IN *DROSOPHILA MELANOGASTER*

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BRCA1-associated protein-1 (BAP1), which is an epigenetic factor, plays an important role in regulating gene expression. BAP1 germline mutation is related to and plays different roles in a variety of human tumorigenesis. Calypso is a homologous gene of BAP1 in Drosophila melanogaster. The physiological and genetic role of Calypso in ocular development during metamorphosis was still less studied. In this work, we found that the knockdown of calypso in D. melanogaster eyes causes a tumor-like malformation. We first dissected the eye imaginal discs of D. melanogaster, and then conducted RNA sequencing analysis which showed that calypso knockdown could affect the activity of insulin signaling pathway. Both the expression of insulin signaling pathway reporter genes and the Akt phosphorylation level revealed that insulin signaling pathway had been intensively activated in the eyes of D. melanogaster by calypso knockdown. We further knocked down certain target genes in insulin signaling pathway in the eyes of D. melanogaster whose calypso had been already knocked down, and found that the akt, rheb, s6k, or upd3 knockdown could rescue tumor-like phenotype to different degrees. Among them, the eyes of the D. melanogaster with akt or rheb knock down were restored to their normal shape. The results suggested that the tumor-like phenotype caused by calypso knockdown in D. melanogaster eyes can be mediated by the hyperactivation of PI3K/Akt/mTOR pathway downstream insulin signaling pathway.

Key words. *Drosophila; tumor-like malformation; Calypso/BAP1; insulin signaling pathway; PcG genes; eye development.*

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ГЕН ГРУПИ POLYCOMB, CALYPSO, РЕГУЛЮЄ РОЗВИТОК ПУХЛИНОПОДІБНОЇ ВАДИ РОЗВИТКУ ОЧЕЙ ЧЕРЕЗ ІНСУЛІНОВИЙ СИГНАЛЬНИЙ ШЛЯХ У *DROSOPHILA MELANOGASTER*

BRCA1-асоційований білок-1 (BAP1), який є епігенетичним фактором, відіграє важливу роль у регуляції експресії генів. Мутація зародкового шляху BAP1 пов'язана з різноманіттям онкогенезу в людини й відіграє в ньому різні ролі. Calypso — це гомологічний ген BAP1 у *Drosophila melanogaster*. Фізіологічна і генетична роль Calypso в розвитку очей під час метаморфоз вивчалася менше. У своїй роботі ми виявили, що нокдаун Calypso в очах *D. melanogaster* спричиняє пухлиноподібну ваду розвитку. Спочатку ми препарували диски зорових нервів *D. melanogaster*, а потім провели аналіз секвенування РНК, який показав, що нокдаун Calypso може впливати на активність інсулінового сигнального шляху. Експресія генів-репортерів інсулінового сигнального шляху та рівень фосфорилювання Akt показали, що інсуліновий сигнальний шлях був інтенсивно активований в очах *D. melanogaster* внаслідок нокдауну Calypso. Далі ми нокаутували певні гени-мішені в інсуліновому сигнальному шляху в очах *D. melanogaster*, у яких Calypso вже був нокаутований, і виявили, що нокаут akt, rheb, s6k або upd3 може різною мірою відновлювати пухлиноподібний фенотип. Зокрема, очі *D. melanogaster* з нокдауном akt або rheb відновлювали свою нормальну форму. Отримані результати свідчать про те, що пухлиноподібний фенотип, спричинений нокдауном Calypso в очах *D. melanogaster*, може бути опосередкований гіперактивацією шляху PI3K/Akt/mTOR нижче за течією інсулінового сигнального шляху.

Ключові слова: *Drosophila*; пухлиноподібна вада розвитку; Calypso/BAP1; інсуліновий сигнальний шлях; гени групи polycomb; розвиток очей.

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