Structural and functional analysis of *Drosophila* organic solute carrier partner 1

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Abstract

OSCP1 is known as a transporter of various organic solutes into cells and also is reported to act as a tumor suppressor protein. Although the possible roles of OSCP1 have been studied with mammalian cell lines, its biological significance in living organisms is not fully understood. In this thesis, I utilized *Drosophila melanogaster* model for functional analysis of *Drosophila* OSCP1 (dOSCP1). In the present study, I found that dOSCP1 could form a dimer and it localizes not only in the plasma membrane but also in the nucleus, endoplasmic reticulum (ER), Golgi apparatus and mitochondria. Moreover, induction of rough eye phenotype was observed in adult dOSCP1-overexpressing flies, likely resulting from a delay in S phase progression and induction of caspase-dependent apoptosis followed by compensatory proliferation. ER stress was also observed in salivary gland of dOSCP1-overexpressing cells. On the other hand, in this thesis, I demonstrated that knockdown of dOSCP1 induced caspase-dependent apoptosis followed by a compensatory proliferation and ROS generation in eye discs. The induction of apoptosis appears to be associated with down-regulation of the anti-apoptotic *Buffy* gene and up-regulation of the pro-apoptotic *Debcl* gene. These effects of knockdown of dOSCP1 lead to mitochondrial fragmentation and degradation, and a shortcoming in ATP production. Furthermore, knockdown of dOSCP1 negatively regulated the EGFR signaling and caused a defect in the cone cell and pigment cell differentiation of pupal retinae. My data indicate that dOSCP1 involves in multiple biological processes such as apoptosis, proliferation, differentiation and ROS generation, and ER stress during *Drosophila* development. The dOSCP1-knockdown flies used in this thesis should provide a useful tool for elucidating functions of OSCP1, pathological mechanisms of the associated diseases, and also finding drug candidates to treat various diseases in which OSCP1 is involved.