Ph.D. projects in progress

1.

Mentor: József Mihály

Doctoral school: SZTE ÁOK Doctoral School of Multidisciplinary Medical Scienses

Ph.D. student: Krisztina Tóth

Title of the research topic: Investigating the mechanisms of neuronal cytoskeleton regulation is Drosophila models

Description of the research topic: Directed axonal growth is known to be strictly dependent on proper coordination of the actin and microtubule cytoskeleton. However, despite of the relatively large number of proteins implicated in the regulation of the actin-microtubule interaction, the cellular details of its mechanisms remained largely unclear. Previously we have shown that Drosophila DAAM (dDAAM) plays an essential role in differentiation of the embryonic nervous system and later on in development of the adult brain. We revealed that dDAAM behaves as a bona fide formin, i.e. it nucleates actin filaments and supports their elongation by remaining processively attached to their barbed ends. In addition we demonstrated that this formin is able to interact with microtubules as well. Using primary neurons, we demonstrated that dDAAM regulates the length and stability of the axonal microtubule bundles. Furthermore, live imaging revealed that dDAAM is required for the proper dynamics of axonal microtubules. Based on these findings, we conclude that dDAAM is an axonal microtubule regulator and a potential candidate to coordinate the actin and microtubule cytoskeleton. Our aim is to combine molecular genetic, biochemical and cell biological methods by using Drosophila neuronal models to unravel the precise mechanisms whereby formins contribute to the coordinated regulation of the axonal cytoskeleton.

2.

Mentor: József Mihály

Doctoral school: SZTE ÁOK Doctoral School of Multidisciplinary Medical Scienses

Ph.D. student: Péter Görög

Title of the research topic: Investigating the molecular mechanisms of sarcomerogenesis

Description of the research topic: During muscle development, de novo formed myosin and actin filaments assemble into the greatly organized sarcomeric structure critical for muscle function. Although sarcomerogenesis clearly involves the formation of novel actin filaments, it has so far been poorly understood how these filaments form. Two key steps of filament formation are nucleation and elongation. However, in muscle cells the essential

actin nucleation and elongation factors, regulating actin filament formation, have not been clearly identified, and thus the mechanism that ensures sarcomeric thin filament assembly remained mysterious. Recently, we found that DAAM family formins, well known actin nucleation and elongation factors in nonmuscle cells, also play an essential role in sarcomerogenesis, whereas others identified the SALS protein as a key regulator of thin filament elongation. Our major objective is to investigate the molecular and cellular mechanisms of thin filament assembly during sarcomerogenesis by the detailed analysis of the functions of DAAM family formins and SALS. We aim to use the combination of genetic, cellular and in vitro assays to reveal the functional properties of these proteins, and to explore their molecular interactions with each other and with the known regulators of thin filament formation. We expect that the complex approach proposed will help us to gain deeper insights into the mechanism of myofibrillogenesis, especially into the mechanism of thin filament formation and the integration of the actin and myosin filament systems.