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Review of the PhD Dissertation of Teresa De Cicco entitled „The role of actin-remodeling proteins Cap2 and Ctnn in the development of neuromuscular synapses”

Neuromuscular junction, also known as motor end-plate, is a place of contact between neuronal system and the active part of locomotor system, skeletal muscle fibers. This structure is present in and essential for all vertebrates and malfunctioning of the neuromuscular junction leads to serious neuromuscular diseases.

Although the motor end-plate was discovered about a hundred years ago and its structure and function have been intensively studied since then, the morphology, plasticity and function of this structure are still not fully understood.

Dr. Tomasz Prószyński and his team have been successfully studying various aspects of functioning and formation of the neuromuscular junction for years.

One of the crucial aspects of the proper functioning of all kinds of synaptic connections is precise regulation of their cytoskeleton morphology and protein composition. The main component of the synaptic cytoskeleton is actin. Actin cytoskeleton is a highly dynamic structure regulated by several proteins with multiple functions. They can stabilize actin filaments but they can also stimulate their growth (polymerization) or shorten their length (depolymerization). They can also induce branching or debranching of the fibrillar actin.

Although the basic information on the regulation of the actin cytoskeleton of the neuromuscular synapse is well documented (or at least we think that it is), the role of many proteins involved in the



interaction with actin within the region of the motor end-plate is still not fully known or even completely enigmatic.

The main goal of Teresa De Cicco studies conducted under the supervision of Dr. Tomasz Prószyński, was to gain an insight into roles of two proteins that are known to regulate the actin cytoskeleton: adenyl cyclase-associated protein 2 (Cap2) and cortactin (Ctnn), in the development/formation of neuromuscular junctions.

A part of results obtained by Mrs. Teresa De Cicco during realization of her project has already been published in renowned journals: Proceedings of the National Academy of Science i Frontiers in Molecular Neuroscience.

In her work, Mrs. Teresa De Cicco used and demonstrated an expert level in a variety of experimental and molecular biology techniques, such as: genetic modifications of mice (preparing of Cap2 and Ctnn KO mice), genotyping, molecular cloning, electroporation, cell culturing and handling (transfection, coimmunoprecipitation, etc.). She also showed an expertise in histological techniques and behavioral tests.

The Dissertation is written in correct academic language, and the extensive Introduction provides the basic information about the subject of the study in a broad physiological context. The Materials and Methods section describes experimental procedures accurately enough to be replicated in any laboratory, and the Results section is precise and exhaustive enough to follow the Discussion and Conclusions. Thus, I have no serious concerns about the Dissertation. It just seems to me that the Conclusions section is too long - it would be clearer for readers if only the most important conclusions were shown. I also think that a subsection (even if very short) which would somehow tie together Cap2 and Ctnn would be useful in the Dissertation. In the Introduction, Ms. Teresa De Cicco nicely described the biochemistry and biology of both proteins and thus, readers know they are actin-cytoskeleton binding proteins, etc. But why did she select these two specific proteins for her studies?

However, these minor objections do not change the fact that Ms. Teresa De Cicco delivered a very interesting and valuable observations and hence, I rate her work very highly. Importantly, she demonstrated the ability to work with animal models and cell cultures, and also mastered numerous techniques of molecular biology and cyto-/histochemistry. I have no doubts that with such a broad

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range of laboratory skills and deep expertise, Ms. Tersa De Cicco will be very valuable asset for any team working in the field of experimental/molecular biomedicine.

In my opinion, Ms. Teresa De Cicco has met all the conditions necessary to obtain the PhD degree.

Therefore, I declare that „Rozprawa doktorska spełnia warunki określone w art. 13 Ustawy z dnia 14 marca 2003 r. o stopniach naukowych i tytule naukowym oraz o stopniach i tytule w zakresie sztuki (Dz. U. nr 65 poz. 595 z późn. zm.)” zgodnie z art. 179 - przepisy wprowadzające ustawę - Prawo o Szkolnictwie Wyższym i Nauce (Dz. U. 2018.0.1669 – ustawa z dnia 3 lipca 2018 r.), and I recommend admitting Ms. Teresa De Cicco to public defense of her doctoral thesis.

At the same time, I am asking the Scientific Council of the Institute of Immunology and Experimental Therapy to consider awarding the Dissertation.

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