



## **Review of dissertation thesis of Mgr. Sukriye Yildirim**

Thesis “ Myosin - PIP2 interaction in the cell nucleus” originated in the IMG Academy of Sciences, in the Department of Biology of the cell nucleus led by Prof. Pavel Hozák.

For a long time, the existence and function of actin and actin motors in the nucleus had been rather controversial. In the 1970s, presence of actin in amphibian oocytes was observed and described as necessary for transcription on salamander lampbrush chromosomes. On the other hand, nuclear actin was in other papers considered to be cytoplasmic contamination or experimental artefact. From that time, cumulating reports confirmed the presence of actin and actin-associated proteins in the nucleus and showed actin involvement in several crucial nuclear processes as transcription, transcription regulation, and chromatin remodelling. The laboratory of Prof. Hozak has significantly contributed to knowledge in this field.

Sukriye Yildirim studied nuclear myosin myosin 1 (NM1) and myosin 1C (Myo 1C) and in her dissertation, she addressed following specific issues: i) which part of the Myo1C/NM1 is responsible for targeting these proteins into the cell nucleus, ii) whether these proteins interact with fosfatidylionositol 4, 5 biphosphate (PIP2), and if so, what are other interacting partners of the lipoprotein complex, iii) whether PIP2 participates on transcription by the DNA-dependent polymerase I, and, finally, iv) whether presence of PIP2 in the nucleoli has any impact on transcription activity of cells.

The dissertation is based on 1 review "Actin complexes in the cell nucleus: new stones in an old field" (Mgr. Yildirim is the sixth of nine authors) published in Histochemistry and Cell Biology (IF = 2.588) and 4 papers, one of which is published in PLoS One (IF = 4.092 (Mgr Yildirim is the second co-author), and the second (in which Mgr. Yildirim is the first author) is accepted for publication in Cell Science (IF = 6.111). Two other manuscripts were not accepted for publishing in time of dissertation submission.

The work is written in English, in a shortened form, where the abstracts are followed by the chapter of Introduction, then, by the chapter "Motivation and objectives" (that effectively highlights the problems addressed). Then, copies of publications and papers prepared for publication follow. For each manuscript, Mgr Yildirim indicated her own

contribution. Finally, the thesis contains short discussion to each addressed problem, Summary and conclusions and short prospects.

In the first paper (PLoS One), the new specific NLS of nuclear myosin 1 (NM1) was identified which is present also in NM1 “cytoplasmic” isoform, myosin 1c (Myo1C). Authors also found Myo1c in purified cell nuclei of mice lacking NM1.

Other three manuscripts deal with PIP2, its distribution in the nucleolus, involvement in Pol 1 transcription and its interactions with actin motors, NM1 and Myo1C.

The introduction is written well, logically and with a minimum of typing errors.

The dissertation thesis is a good typographic quality

Attached publications indicate ability of the candidate to carry out valuable scientific research. Hopefully, two, yet unpublished, manuscripts will be successfully published soon.

Comments and questions:

Page 21: Phosphatidylinositol transfer protein abbreviation is PITP

What is PITB?

NM1 is suggested to have roles in transcription and chromatin remodelling. What is a phenotype of NM1 knock out mice?

PIP2 is engaged in many processes and interactions. It can bind specifically proteins via interactions with protein domains of known structure but it can be bound also to proteins non-specifically by electrostatic interactions. I suppose, it may be very difficult to distinguish between functional and contaminant binding of PIP2.

Do you think that the the presence of PIP2 in nucleolus is the result of its local synthesis or specific binding or electrostatic sequestration?

In conclusion:

Mgr. Yildirim demonstrated a strong knowledge of her research field and a high-level experimental skill. The high level value of the thesis is proved by two publications with cumulative IF = 10, 2. The candidate is also the first author of two other manuscripts prepared for publishing and co-author of 1 published review.

Therefore, I strongly agree on the **acceptance** of this thesis for further procedures of PhD title award.

Prague, May 24, 2013

Doc. RNDr. Jitka Forstová, CSc.