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věc: disertační práce studentky Mgr. Miroslavy KARDOŠOVÉ (školicelka Meritxell Alberich Jorda, Ph.D.)

## POSUDEK DISERTAČNÍ PRÁCE

It was my pleasure to read dissertation thesis of Dr. Miroslava Kardošová entitled: „Regulatory mechanisms in normal and malignant granulopoiesis“. The Thesis summarizes 3 major original articles all co-authored by the candidate. Publications are in respected Journals of high impact such as Haematologica, Nature Communications or J. Biol. Chem.

A 172-page thesis consists of introductory part, aims, results, conclusions and attached are major publications. Briefly, the work describes gene knockout approach to test a role of *Cebpg* in granulopoiesis that showed redundancy of this gene. The EVI2B regulation by CEBPA was demonstrated in AML cell line and using *Cebpa* k.o. mice. Role of miR-143 in granulopoiesis and its prognostic impact for better outcome in AML was also elucidated.

The work has many approaches and is well explained and defended by publications in peer-reviewed journals. It also stands solid in the thesis and all data were commented efficiently and I had no problem in understanding the logical explanation and interpretation of the experimental parts.

My questions are as follows:

1. how other *Cebp*'s factors react either on mRNA level or by other means to the loss of *Cebpg* - do they compensate?
2. it has been demonstrated that significantly increased expression of miR-143 (and miR-145) was observed in del5q- patients as these miRs are lost within the deleted region. Del5q is also seen in AML patients. Did you study also the patients or cells with del5q?
3. it has also been shown that knockdown of miR-143 (and miR-145) in cord blood CD34+ cells resulted in increased erythroid (progenitor) activity - have you made some such observations e.g. in K562 erythroleukemia cells?

Overall the PhD thesis is very well presented and upon answering my points for discussion I recommend this work for PhD defense and suggest the decision to the PhD committee to approve awarding the PhD title after the candidate's name.

—  
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