

Supervisor's Evaluation - PhD thesis of Kateřina Voračová

Kateřina came to our laboratory six years ago with the aim to study pro-apoptotic effects of novel secondary metabolites isolated from cyanobacteria. At that time, our small working group was focused on isolation and characterization of compounds with general cytotoxic effect mainly from the toxicological point of view. Katerina had in some aspects of the work (e.g. testing new methodologies and protocols) difficult starting position. However, her independent interest in physiology of cell death and cell death machineries led to involvement of new experimental approaches in our laboratory and formulating of novel hypothesis.

In the first part of the study, Kateřina participated in two screening studies aiming to characterize general cytotoxic effects of crude cyanobacterial extracts as well as their pro-apoptotic effects. These studies resulted in two scientific papers in which Kateřina performed part of the experimental work (paper 1), or was fully involved in data interpretation, writing and formulation of the manuscript (paper 2). Although these data are not published in high impact-factor journals, I highly appreciate them, mainly because the results and experience gathered will be helpful for future natural product screening in our laboratory (and I believe that will be useful also for many other researchers). After screening part, Katka unfortunately experienced several failures to recover bioactive compounds responsible for the effect of the whole crude extract. Unsuccessful trials to recover compounds with proapoptitic effects from crude extracts may be caused by additive and multiplicative effects of several compounds present in the extract, which in combination are leading the cell to apoptosis. Thus the failures should be rather attributed to the complexity of the extracts rather than experimental mistakes. Finally, we have decided to characterize pro-apoptotic effect of a novel organic compound discovered in our laboratory (nocuolin a). Within this largest portion of experimental work, Katka characterized the dynamics, efectivity and symptoms of nocuolin induced cell death. In the mainframe of this study she also visited two excellent laboratories (British Columbia Cancer Agency and Medical University of Innsbruck) where she performed first insights in the characterization of signaling behind NoA-induced cell death and worked on characterization of nocuolin potency *in vitro*. Unfortunately, many data stayed unpublished till now, mostly due to the low yield of the compound hampering the isolation of its sufficient amounts. Much more experiments are needed in order to prove the theories about role of autophagy in nocuolin induced cell death and effect of nocuolin of the mitochondrium.

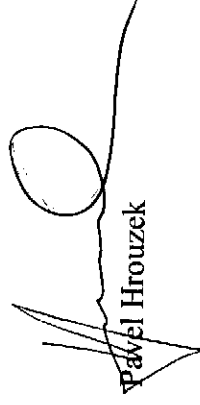
Recently obtained higher amount of the compound, however, will allow Kateřina to finish some of these experiments and uncover the answer for some of these questions.

It is also worth to mention that Kateřina was supervising one successful bachelor thesis (and co-supervising master thesis) of Kateřina Vicková, which led to discovery of another compound inducing regulated cell death in human cells in nanomolar range (unfortunately this study can not be a part of this thesis in current stage).

Finally, I would like to say that Kateřina is a valuable member of our team. She performed a good piece of work, although there were many complications during her study. In her thesis she summarize basic knowledge about cell death and various cell death machineries together with her opinion on isolation of novel compounds from natural resources (mainly cyanobacteria). As I was involved in preparation of the thesis, I can say that Kateřina prepared it thoroughly and based on its content and quality I fully support its best evaluation.

I wish her good luck in next scientific carrier and less of self-criticism and less of stubbornness.

In Třeboň 31th May



Pavel Hrouzek