

FIRST PERSON

First person – Karolina Losenkova

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping early-career researchers promote themselves alongside their papers. Karolina Losenkova is first author on 'Compartmentalization of adenosine metabolism in cancer cells and its modulation during acute hypoxia', published in JCS. Karolina is a PhD student in the lab of Gennady Yegutkin at Medicity Research Laboratory, University of Turku, Finland, investigating the role of purine-converting enzymes in tumorigenesis.

How would you explain the main findings of your paper in lay terms?

Owing to high plasticity, tumor cells are capable to adapt their metabolic pathways under different environmental challenges. In particular, hypoxia might directly affect extra- and intracellular concentrations of ATP and other purinergic metabolites, in cancer cells and the tumor microenvironment. This could result in drastic changes in cancer cell motility, signal transduction, bioenergetics and invasiveness. We have shown that the purine metabolism of highly invasive breast and prostate cancer cells is the dynamic process that is coordinated by a broad spectrum of extracellular purine-converting enzymes, equilibrating nucleoside transporters and intracellular nucleotide kinases. The exposure of cancer cells to acute hypoxia triggered upregulation of ecto-5'-nucleotidase (CD73) without altering other enzymes. We have additionally shown the inhibitory effects adenosine has on early tumor establishment in a receptor-independent manner. Thus, for further studies it is important to keep in mind that purine metabolism is a complex pathway that plays a significant role in the maintenance of cancer cells plasticity.

Were there any specific challenges associated with this project? If so, how did you overcome them?

Recent research has focused mostly on the roles of 'classic' inactivating purine ectoenzymes, e.g. nucleoside triphosphate diphosphohydrolase-1 (CD39) and ecto-5'-nucleotidase (CD73). CD39 and CD73 are considered to be a promising target for cancer immunotherapy, with several anti-CD73 and anti-CD39 antibodies being tested in clinical trials for cancer treatment. Nevertheless, it has now become clear that extracellular purine turnover depends on the more-complex interplay between ectoenzymatic pathways. There are several, currently underappreciated, alternative routes; in particular, the ATP-inactivating pathway through nucleotide pyrophosphatase/phosphodiesterase-1 (NPP1, also known as ENPP1) activity and reverse ATP resynthesis by the members of the nucleoside diphosphate kinase (NDPK) family and by adenylate kinase. In addition, the study of intracellular purine metabolism, in terms of cancer progression, has been abandoned. Therefore, the goal of our study was to consider ATP and adenosine homeostasis as a complex network by paying special attention to dynamic and interrelated extra- and intracellular pathways.

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Karolina Losenkova

When doing the research, did you have a particular result or 'eureka' moment that has stuck with you?

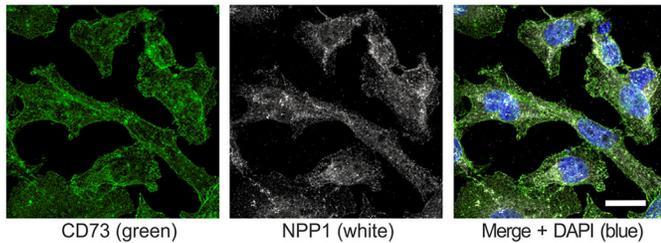
Personally, I am amazed by the complexity and diversity of our cells. The first project I was involved in was about the effects of hypoxia on purine metabolism in vascular endothelial cells. Interestingly, in contrast to vascular endothelial cells, ectoenzyme CD39 does not play an exclusive role in hydrolyzing ATP via ADP into AMP in breast and prostate cancer cells. By contrast, they express another ectoenzyme, NPP1, capable of converting ATP into AMP and PP_i. Therefore, this alternative pathway might be used by cancer cells to bypass CD39 cancer therapeutics.

Why did you choose Journal of Cell Science for your paper?

Journal of Cell Science is an international journal with high quality standards for their research papers. The scientific articles published in the journal cover a wide range of cell biology topics. In addition, I am grateful for such a great opportunity for young scientists to promote their research and themselves.

Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

The work environment is an important component for scientists' well-being. I am grateful to be part of the great and very supportive team led by Professor Sirpa Jalkanen. Being a PhD student, it is crucial to have mentors who have time to guide you and provide support whenever you need it. I won the lottery to have such amazing people as my supervisors. Both of them, Docent Gennady Yegutkin and Professor Sirpa Jalkanen, are experts in their fields, who gladly share their knowledge and experience. I also want to emphasize that I feel their support not only in work-related aspects. Without this enormous help, my experience in living and doing research abroad wouldn't be that smooth and enjoyable.



Confocal images showing the expression levels of CD73 and NPP1 in human breast cancer MDA-MB-231 cells. Scale bar: 20 μ m.

What motivated you to pursue a career in science, and what have been the most interesting moments on the path that led you to where you are now?

I would never have imagined that science would be a part of my life, and a set of circumstances led me to the place where I am now. But, certainly, I do not regret choosing this path with its ups and downs. I have been working in two different laboratories in Russia and Finland. I find it is very interesting to compare the scientific life, depending on the work environment and the mentality. You can learn a lot by picking up the strongest points of these different experiences.

Who are your role models in science? Why?

It is challenging to choose someone in particular. I am inspired by people who feel that science is not their profession but their life

style. And I do not talk only about highly successful scientists but everyone who does their research with passion. Luckily, I have always been surrounded by this type of person.

What's next for you?

I am still only half the way through my PhD degree. In addition to the main research on roles of purine-converting enzymes in tumorigenesis, I am also involved in several side projects. For instance, purine-converting enzymes may be involved in other pathophysiological conditions, such as Alzheimer disease and ocular diseases. I am looking forward to getting the results, which might facilitate findings of new effective purine-based therapeutic possibilities.

Tell us something interesting about yourself that wouldn't be on your CV

In my free time, I like to dance lindy-hop and listen to rock music from the 70s. Now, since our daily life is being affected by coronavirus, I have more spare time to finally learn playing the ukulele. It has a very cheerful sound that lifts your mood, no matter what kind of results you have had.

Reference

Losenkova, K., Zuccarini, M., Karikoski, M., Laurila, J., Boison, D., Jalkanen, S. and Yegutkin, G. G. (2020). Compartmentalization of adenosine metabolism in cancer cells and its modulation during acute hypoxia. *J. Cell. Sci.* **133**, jcs241463. doi:10.1242/jcs.241463