

INTERVIEW WITH THREE KUFFLER AWARDEES

Two years have passed after the first announcement of the winners of the Stephen W. Kuffler Research Scholarship and by now altogether 16 young researchers have received Kuffler awards. We asked two winners of the first year, **Júlia Batki** and **Márton Kolossváry**, and **Anna Molnár** awarded in 2014 about their progress and how the Kuffler Fellowship have helped their progress.

Currently **Júlia Batky** is a PhD student in the Institute of Molecular Biotechnology (Vienna, Austria), in the laboratory of Julius Brennecke, **Márton Kolossváry** and **Anna Molnár** are still medical students at the Semmelweis University, Budapest. Although all three young researchers are very determined and science is a major part of their life, their answers reveal not only the differences in their personalities, but how they see the world around them.

- *What are your newest achievements?*

Júlia Batki

- Specifically, I am very much interested in a family of small RNAs that has been discovered only recently and plays an essential role in germline development. Piwi-interacting RNAs (piRNAs) mediate silencing of the deleterious transposable elements (TE), in order to maintain integrity of the germline genome. piRNAs guide Argonaute proteins of the PIWI-clade to complementary TE transcripts. Nuclear Piwi proteins have been shown to mediate transcriptional gene silencing of TEs, which is accompanied by heterochromatin formation with H3K9 trimethylation being the central hallmark.

In my research I use *Drosophila melanogaster* (fruit fly), the leading model system in the field, to investigate the mechanism of piRNA-guided transcriptional silencing. In our recent study (*Sienski, Batki & Senti et al, 2015. Genes and Development*) we have characterized a novel factor, CG9754/Silencio as an essential piRNA pathway factor that is required for Piwi-mediated transcriptional silencing. Silencio interacts with Piwi and interestingly its artificial recruitment to nascent RNA induces transcriptional silencing that is independent of Piwi. However, Silencio-

mediated repression requires the H3K9 methyltransferase Egless/SetDB1. Based on our results, we suggest that Silencio acts as a linker between the sequence specificity factor Piwi and the cellular heterochromatin machinery.

Márton Kolossváry

- As a member of the Cardiovascular Imaging Research Group at Semmelweis University, my research area is non-invasive imaging of coronary atherosclerosis. In the last year, I was busy with the statistical analysis of one of our projects, where we scanned 101 twin pairs with a CT to get precise information regarding their cardiovascular health. With twin studies, the variation between the siblings can be decomposed to environmental and genetic factors. With our research we will be able to define to what extent environmental and genetic factors contribute to coronary atherosclerosis. In the last year, I received multiple awards at Semmelweis University's Scientific Congress, and also reached 2. place at the National Scientific Congress. I was also co-author of 4 international publications, and also held oral and poster presentations at international congresses. This year I also received the Pro Scientia gold medal.

Anna Molnár

- My research topic lies in tumor biology, more specifically in the mTOR (mechanistic target of rapamycin) kinase which is a central controller of a wide range of cell functions and plays a crucial role in tumor growth and cancer development. Inhibition of mTOR has become a potential therapeutic strategy. We examined the molecular basis of resistance to mTOR inhibitors in colon carcinomas. Our results are now under review, we described that high activity of mTORC2 complex may cause resistance to specified mTOR inhibitors and in situ quantitative determination of active mTORC1 and C2 complexes could be used as diagnostic method to define the appropriate therapy for each patient. We also identified that combination therapy of mTOR and EGFR inhibitors in colon carcinoma cell lines increases the inhibition of proliferation compared to their individual effects. These results confirm the need for combination therapy in cancer treatment and it may decrease the resistance related issues to mTOR inhibitors. My other research project concerns the examination of specified microRNA expression levels in colon carcinomas. MicroRNAs can regulate gene expression and influence the tumor growth and development. We are identifying whether the exchanged expression of microRNAs

originates from the tumor epithelial cells or from the tumor stroma where numerous distinct cell types can be found. It is important to know as the microenvironment of the tumor cells has dominant impact on tumor development. It would also have a fundamental significance in describing which microRNA can be used as a cancer diagnostic indicator.

We have already found special microRNAs which expression level is much higher in the tumor stroma than in the tumor epithelial cells, in comparison to normal tissues as well. We are now characterizing this cell-type-specific microRNA expression in details.

- *What is your recent goal?*

Júlia Batki

- At the moment, I am investigating the function of additional factors that are essential for Piwi-mediated silencing. My main aim is to gain more mechanistic insights into small RNA-guided gene silencing and heterochromatin formation via using various approaches, such as genetics, biochemistry and high-throughput sequencing technologies. My studies will greatly contribute to our knowledge of small RNA-guided transcriptional silencing in animals. As strong parallels exist between fly and mammalian piRNA pathways, my results promise to have far-reaching implications for the understanding of this fascinating process in humans.

Márton Kolossváry

- In the next year I'm going to finish my medical education at Semmelweis University, and also my Complementary studies at Pázmány Péter Catholic University – Faculty of Information Technology and Bionics. After my graduation I want to start a PhD at Semmelweis University. I would also like to expand my knowledge in statistics, and complex data analysis.

Anna Molnár

- My current scientific interest is about molecular genetics and developmental biology but I'm open-minded for other themes as well. I'm really interested in the epigenetic (de)regulation of development and aging. I want to deepen my knowledge in genetic methods and go into detail about the mechanisms and effects of the (post)transcriptional regulatory of gene expression. I would also like to try myself in other field of life sciences in order to broaden my scientific view.

I need to get experiences in new research projects so I want to join new research teams in Hungary and abroad as well. I would strongly like to take some research and study abroad.

- *What was the impact of Kuffler Fellowship on your career?*

Júlia Batki

- The Kuffler Fellowship provided me excellent financial support that I took as a unique opportunity to fund a short-term internship with the main goal to gain more research experience at a cutting-edge research institute. Therefore, I applied to the Friedrich Miescher Institute (Basel, Switzerland) and got accepted to the laboratory of Marc Buhler. There, I was involved in a research project investigating the mechanism of small RNA-guided heterochromatin formation in *Schizosaccharomyces pombe* (fission yeast). Besides getting acquainted with a new model system and becoming skilled in many techniques, I contributed to a study that describes the role of the Paf1 complex in building epigenetic memory (Kowalik & Shimada et al, 2015. Nature).

Márton Kolossváry

- Being one of the first to receive the Kuffler Fellowship is a great honour! In applications it is always a great advantage to be awardee.

Anna Molnár

- Kuffler Fellowship is far more prestigious than I have thought before and consequently it affected my career beyond my expectations. At my university, many professors whom I have not known before congratulated me and even the Rector has sent me an official congratulatory letter. Thanks to the Kuffler Fellowship, I became renowned not just at my university but at other research institutes as well and I established professional contacts. I also gained encouragement and self-confidence from this support to continue my dedicated research. The Fellowship confirmed me in that hard work will fructify. Through this professional backing, I went on doing research and I presented my two projects at the National Scientific Students' Associations Conference (OTDK) in April. I won the First and the Second Prize in different sections and the Special Prize for the most outstanding contestant. I got more scholarships and

in November the Pro Scientia Gold Medal and the Professor Genersich Award. In spite of these appreciations, I had doubts and questions about my future scientific career. I asked Professor Nusser, the chair of the Kuffler Foundation about my situation and he helped me through a personal consultation. I am grateful for his advice.

- *What do you think about the effectiveness of the present supporting system in science?*

Júlia Batki

- In my opinion, there is an increasing number of - but still very few - funding possibilities for talented young Hungarian scientists either to support their everyday life or to be used for short/long-term fellowships abroad. I strongly believe that both are essential in order to have continuous development and to become a successful researcher in the life sciences. The Kuffler Fellowship is a wonderful opportunity, which gives this support. In addition, its fellows become a member of an alumni system, which I hope will continue and create a great network that is very rare at the moment.

Márton Kolossváry

- As a medical student, I have little experience with the supporting system in science. Seeing my supervisors, find funding for research is a hard and time consuming project, which could be used for research.

Anna Molnár

- As a student, I saw just a little segment of this supporting system in reality. I have experienced the high competition in science and in research. I think most of the financial and professional supports are really based on the high-quality scientific performance but it's not easy to succeed from an Eastern Europe country. In my view, the professional appreciation is more important for a researcher in Hungary, as the salary and research finance is much lower than abroad.