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FIRST PERSON

First person – Ekaterina Migunova

First Person is a series of interviews with the first authors of a selection of papers published in Disease Models & Mechanisms, helping early-career researchers promote themselves alongside their papers. Ekaterina Migunova is first author on 'ELAC2/RNaseZ-linked cardiac hypertrophy in *Drosophila melanogaster*', published in DMM. Ekaterina is a PhD student in the lab of Edward Dubrovsky at Fordham University, Bronx, NY, USA, investigating the role of *ELAC2* mutations in cardiomyopathy.

How would you explain the main findings of your paper to non-scientific family and friends?

I study a heart disease called cardiomyopathy associated with mutations in the *ELAC2* gene. Babies born with such mutations die from heart failure before their first birthday. To date, no studies have been done to investigate how these variants of the *ELAC2* gene are causing such severe heart defects. In my research, I model ELAC2-linked cardiomyopathy in fruit flies. Mutations of the fly version of the *ELAC2* gene have the same effect in flies as they do in humans; they cause early death, heart wall thickening and reduction of heart contractility. These findings provide the first experimental evidence that the severe heart damage in human patients is indeed caused by the *ELAC2* mutations and not by any other factor. In addition, I have found that mutant fly hearts exhibit fibrosis, increased cardiomyocyte (heart cell) ploidy and increased number of cardiomyocyte nuclei. The last finding opens up the possibility that the stress associated with mutations results in the heart cells either replicating or forming two nuclei per cell instead of one. This is exciting because neither fly nor human heart cells are known to proliferate during adult life and my finding could uncover a previously unknown mechanism. Altogether, these findings provide more information about the heart damage associated with *ELAC2* mutations. I further plan on using the fly model that I generated to study cellular processes underlying this cardiomyopathy.

"Having this knowledge will help not only to increase the chances of diagnosing heart diseases, but could also potentially lead to a targeted treatment."

What are the potential implications of these results for your field of research?

These results could potentially lead to inclusion of the *ELAC2* gene in genetic screens for predisposition to heart disease. Having this knowledge will help not only to increase the chances of diagnosing heart diseases, but could also potentially lead to a targeted treatment.

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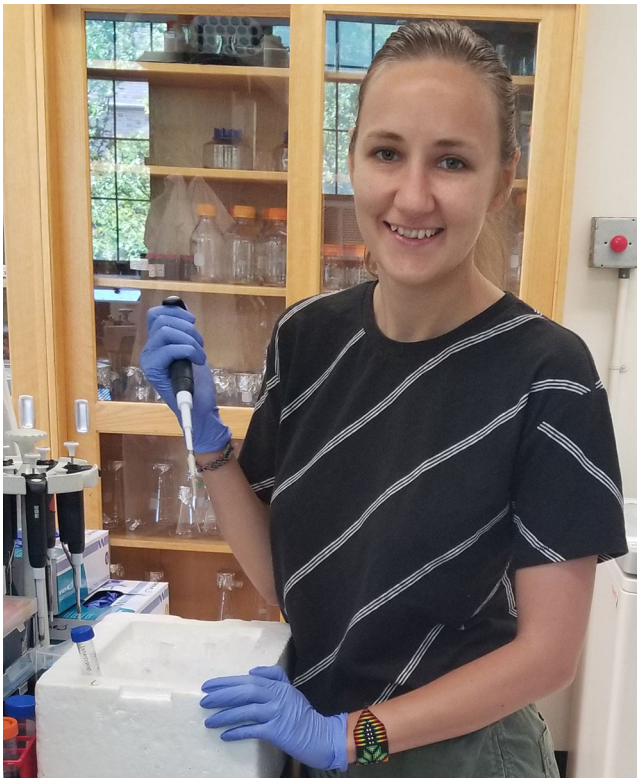

Ekaterina Migunova

"…I always have to convince other people that the similarities between fly heart and human heart are striking."

What are the main advantages and drawbacks of the model system you have used as it relates to the disease you are investigating?

The main advantage of the *Drosophila* fruit fly as a model system is the multitude of genetic tools that allows modification of the fly genome to introduce the desired mutations or markers with ease and in a relatively short time. The only drawback I can think of is that it is not a mammal, so I always have to convince other people that the similarities between fly heart and human heart are striking.

What has surprised you the most while conducting your research?

I think that the great similarity of the symptoms associated with *ELAC2* mutations between humans and flies was very surprising to me. When, for the first time, I saw a hypertrophied heart wall in mutant flies, I was like 'Woah, I can't believe that it actually worked!'.

What do you think is the most significant challenge impacting your research at this time, and how will this be addressed over the next 10 years?

Modeling human heart diseases in flies is a relatively recent trend; therefore, there are not too many tools yet to study the anatomy and

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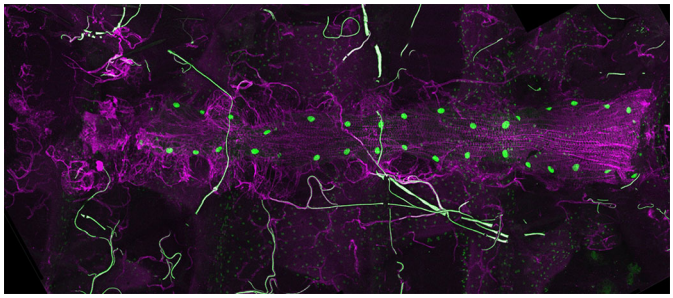

The *Drosophila* adult heart expressing nuclear localized 4xtinC-GFP (green channel) and stained with anti-pericardin, a cardiac-specific extracellular matrix constituent (purple channel).

physiology of fly heart. Yet, I believe as it becomes convincingly clear that the fly heart is an excellent model system for human pathologies, more instruments and methods will be developed to allow for easy diagnosis.

What changes do you think could improve the professional lives of early-career scientists?

I think increased government funding would allow early-career scientists to pursue their passion.

What's next for you?

After defending my thesis, I will be looking for jobs in gene therapy industry. I am excited to apply my skills and knowledge to help develop treatments for people suffering from various ailments.

Reference

Migunova, E., Theophilopoulos, J., Mercadante, M., Men, J., Zhou, C. and Dubrovsky, E. B. (2021). ELAC2/RNaseZ-linked cardiac hypertrophy in *Drosophila melanogaster*. *Dis. Model. Mech.* **14**, dmm048931. doi:10.1242/dmm.048931