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FIRST PERSON

First person – Christin Bissig

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. Christin Bissig is first author on 'The PIKfyve complex regulates the early melanosome homeostasis required for physiological amyloid formation', published in JCS. Christin conducted the research described in this article while a postdoc in Dr Guillaume van Niel's lab at the Institut Curie, Paris Sciences & Lettres Research University, France. She is now a postdoc in the lab of Andreas Mayer at Department of Biochemistry, University of Lausanne, Epalinges, Switzerland, investigating the molecular mechanisms of intracellular membrane trafficking.

Christin Bissig

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

Our skin and eyes are protected against harmful sunlight by a dark pigment, called melanin. The production of melanin is a harmful process; therefore, it is confined to a specific place, called the melanosome, within pigment cells. Like in a warehouse, melanin is stored on a scaffold, which is composed of the protein PMEL. However, we still do not understand how this scaffold is built up within melanosomes. In our work, we find that a protein complex called the PIKfyve complex controls the formation of this scaffold and therefore pigment production. Like a master builder, PIKfyve regulates the import and export of PMEL building blocks to assure optimal conditions for PMEL scaffold assembly. Interestingly, the PMEL scaffold resembles very much those protein scaffolds that aberrantly assemble in the brain and cause neurodegenerative diseases like Alzheimer's disease. Thus, future work will show whether PIKfyve may play analogous roles in scaffold assembly during disease.

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

We quickly had good evidence that inhibition of PIKfyve activity impairs the formation of PMEL fibrils within melanosomes. The main challenge was then to find out why. While we knew that fibril formation requires PMEL sorting and cleavage by proteases, the process of fibril assembly remained a black box. As PIKfyve has crucial roles in lysosome functions in non-specialized cells, we first thought that the observed defect in PMEL fibril formation could arise from lysosomal dysfunctions that would impair PMEL proteolysis. However, all our data showed that lysosome functions are unaffected by PIKfyve inhibition in pigment cells. Thus, we were on the wrong track. We then changed strategy and decided to do electron microscopy experiments on high-pressure frozen cells to optimally preserve membrane ultrastructure with the hope of seeing morphological changes in endosomes or melanosomes that are induced by PIKfyve inhibition. It worked out, and we found that PIKfyve activity is required for membrane remodeling of the earliest stage of melanosomes. This experiment brought us back on track and we could then go on and describe how these morphological changes affect PMEL abundancy and fibril assembly.

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

As mentioned above we were for a long time looking for lysosomal dysfunctions, because in the literature PIKfyve is described to act on lysosomes. Thus, all our negative results did not fit with what was known. However, when we found that PIKfyve is a major player in early melanosome maturation everything started to make sense. We could then show that PIKfyve plays similar functions in maturation of melanosomes and lysosomes in specialized and non-specialized cells, respectively. Thus, our findings indicate that pigment cells employ a conserved mechanism to generate their specialized organelles.

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

We chose Journal of Cell Science because we wished to publish in a journal with an excellent reputation and a wide readership with the goal to spread our findings as broad as possible within the cell biology community.

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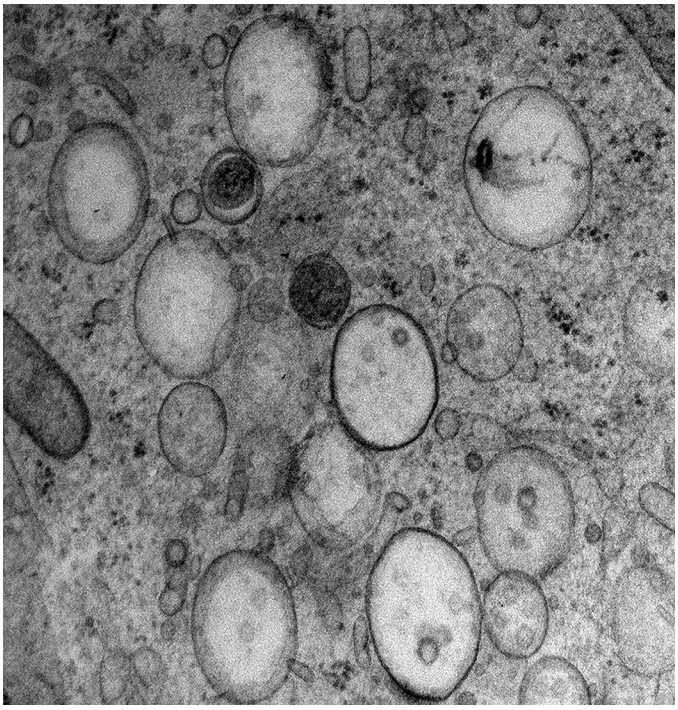

Electron microscopy picture of a high-pressure frozen pigment cell showing enlarged early melanosomes after PIKfyve inhibitor treatment.

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

Dr Guillaume van Niel was a great and very enthusiastic mentor for this work. He managed to perfectly find the balance of guiding, while giving me space to work independently. I have learned from him that a scientist must be open-minded and courageous enough to also pursue unconventional ideas.

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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?

My main motivation for pursuing a career in science is my curiosity. I am a very curious person and I wish to understand how nature works. Since the beginning of my studies, I have been fascinated about the molecular mechanisms cells employ to make our life possible. Even though research can be very frustrating at some moments, I really enjoy working as a researcher. I think it is a very enriching and exciting job that is intellectually challenging, demands creativity and gives the possibility to learn something new every day.

What's next for you?

Since I enjoy working at the bench I moved on to do another postdoc. After working many years with mammalian cells, I am now discovering the ease and power of yeast.

Reference

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