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FIRST PERSON

First person – Arthur Lensen and Margarida C. Gomes

First Person is a series of interviews with the first authors of a selection of papers published in Disease Models & Mechanisms, helping researchers promote themselves alongside their papers. Arthur Lensen and Margarida C. Gomes are co-first authors on 'An automated microscopy workflow to study *Shigella*–neutrophil interactions and antibiotic efficacy *in vivo*', published in DMM. Arthur conducted the research described in this article while an MSc student in Serge Mostowy's lab at the London School of Hygiene and Tropical Medicine, UK. He is now a PhD student in the lab of Jost Enninga at Institut Pasteur, Paris, France, investigating host-pathogen interactions at the cellular and molecular level. Margarida is a research fellow in Serge Mostowy's lab at the London School of Hygiene and Tropical Medicine, UK, and works with the zebrafish infection model to study host-pathogen interactions, focusing on trained innate immunity.

Arthur Lensen

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

Shigellosis is a widespread disease triggered by the bacterium *Shigella*, causing approximately 200,000 deaths every year worldwide, and is particularly dangerous to young children. Several treatments are available, such as antibiotics, but become less and less efficient every year, as antibiotic-resistant bacteria spread. There is a need to discover new therapies against shigellosis, but studying this disease in animals is a complex task as mice, the most common animal model, are not naturally susceptible to the disease. To study *Shigella* interaction with immune cells, the Mostowy lab uses zebrafish larvae. An important feature of this model is that larvae are transparent and allow non-invasive visualisation of what is happening inside using fluorescence microscopy. We took advantage of this feature to develop a new microscopy and image analysis workflow to image, detect and count immune cells, that had been made fluorescent. The cells we focused on were neutrophils, a first barrier of defence in zebrafish (and humans) against infection, which are professionals at eating and killing *Shigella* bacteria. Using our novel workflow, we discovered that antibiotics and neutrophils work together to clear *Shigella* in zebrafish larvae.

"We developed LenCell, a Fiji/ImageJ macro (freely accessible on GitHub) that is easily adaptable to answer a wide variety of research questions involving zebrafish host-pathogen interactions."

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

The method we developed in this work will allow researchers to screen for interactions between pathogens, immune cells and antibiotics *in vivo*. The use of high-throughput microscopy is important to maximise the number of events captured. However, the high volume of images and data generated requires a fast and efficient method to analyse the data. To address this, we developed LenCell, a Fiji/ImageJ macro (freely accessible on GitHub) that is easily adaptable to answer a wide variety of research questions involving zebrafish host-pathogen interactions. The results we obtained with LenCell clearly demonstrate how crucial it is to test antibiotic efficiency *in vivo* and how different strains of *Shigella* can behave very differently under similar conditions. Fortunately, the workflow we developed using LenCell can help to better characterize and understand these differences.

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

Zebrafish larvae are very useful models to study *Shigella*-neutrophil interactions, and larvae are easily amenable to high-throughput image analysis. Zebrafish are easy to maintain and handle, relatively easy to inject, have a fast development and are optically transparent, allowing us to directly and non-invasively follow *Shigella* infection from the level of the single cell to the whole organism.

Considering that the zebrafish genome is approximately 70% homologous to that of humans, a drawback may be that they may not

Arthur Lensen's contact details: Institut Pasteur, 25-28 rue du Docteur Roux, 75015, Paris, France.
Margarida C. Gomes's contact details: London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK.
E-mail: arthur.lensen@pasteur.fr; margarida.castro-gomes@lshtm.ac.uk

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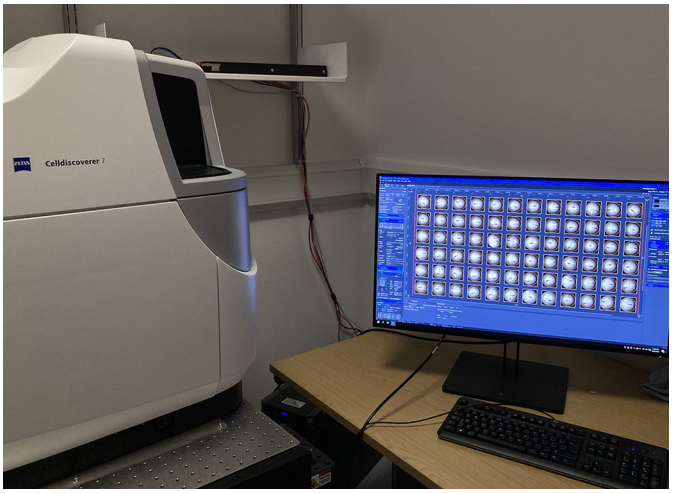
Margarida C. Gomes



View of the Zen software used to control the CD7 microscope.

The software displays the view of zebrafish larvae in the wells of a 96 well plate, before imaging.

fully replicate human disease. Moreover, in our infection model, we are injecting *Shigella* into the larvae's hindbrain ventricle, which is different to the human gut (e.g. no intestinal epithelial cells).

What has surprised you the most while conducting your research?

A.L.: This internship in Serge Mostowy's lab, with Margarida as my primary supervisor, allowed me to discover several different worlds. I previously did an internship in Jean-Marc Ghigo's lab (Institut Pasteur) and got an introduction to the world of zebrafish, but this project in London allowed me to really dive in and discover in detail many aspects of this model organism and how 'fish people' work from day to day. I also discovered the universe of automatic image analysis, which was completely unknown to me before, and opened many doors for my current research project. I never realized before how powerful image analysis could be.

M.C.G.: This project was initially the integration of the use of high-content imaging with the zebrafish model in the lab, to analyse the interaction of different *Shigella* strains and neutrophils. However, with the introduction of antibiotics into the system, it became a lot more interesting. We have now opened a new string of questions regarding the proper use of antibiotics in the clinical setting and how we can maximise the antibiotic impact by understanding its effect on the immune system.

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?

A.L.: At the time of my internship in the lab, the main challenge was working during the COVID-19 pandemic. COVID-19 policies in the UK were very strict, especially for people vaccinated abroad. I remember having many issues working efficiently, between the mandatory quarantines, COVID-19, and being a contact case. But fortunately, the highly positive atmosphere in the lab allowed me to forget a bit about this issue. I think now that we have experienced this pandemic, and as remote working has become more of a norm, we will be more prepared in case such an event happens again.

M.C.G.: The biggest scientific challenge at the moment is antimicrobial resistance (AMR), which needs to be addressed in under 10 years. Surpassing this will require scientists to think outside the box and get creative, as bacteria are very quick at outsmarting us! We hope that continuing our work with the zebrafish model and taking advantage of newer and better tools (such as high-resolution microscopes) can bring us closer to an answer.

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

A.L.: As I am just beginning my career in science, I probably do not realise yet all the ways by which the professional lives of scientists could be improved. The main issue I can see is that there is a serious lack of financial support for scientists, scientific structures and institutes, at least in France and in the UK. Some young scientists are struggling and will struggle even more in the future because of this issue, and this will affect their career and life choices. This also affects the quality of their science, as some of them spend a significant amount of time looking for money instead of doing what they would prefer to do: think about science.

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M.C.G.: Early-career researchers would greatly benefit from more support in their transition to independence. This step is the start of a journey where you are responsible for a team, and you need to wear different hats – the scientist, the manager, the mentor, and whatever else is needed to ensure your vision for the project. Importantly, and probably the major obstacle to the process, available funding is highly competitive and limited.

What’s next for you?

A.L.: After my internship in Serge Mostowy’s lab, I did an internship in Athanasios Typas’ lab at the European Molecular Biology Laboratory (EMBL) and started my PhD in September 2022 in Jost Enninga’s lab at Institut Pasteur, where I am still working on *Shigella*, but on a different topic. I am now focusing on the proteins this bacterium hijacks while invading its host cell and doing lots of microscopy and molecular biology. This is exciting, and I plan to learn as much as possible during these years of training while trying to make great discoveries. In the long term, I would like to try and do a postdoc and stay in academia.

M.C.G.: I have developed a trained immunity model in zebrafish as part of my postdoctoral training, and I am now completing this project. I am planning to transition from a postdoctoral researcher to an independent academic, continuing to study host-pathogen interactions using the zebrafish model.

Reference

Lensen, A., Gomes, M. C., López-Jiménez, A. T. and Mostowy, S. (2023). An automated microscopy workflow to study *Shigella*–neutrophil interactions and antibiotic efficacy *in vivo*. *Dis. Model. Mech.* **16**, dmm049908. doi:10.1242/dmm.049908