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FIRST PERSON

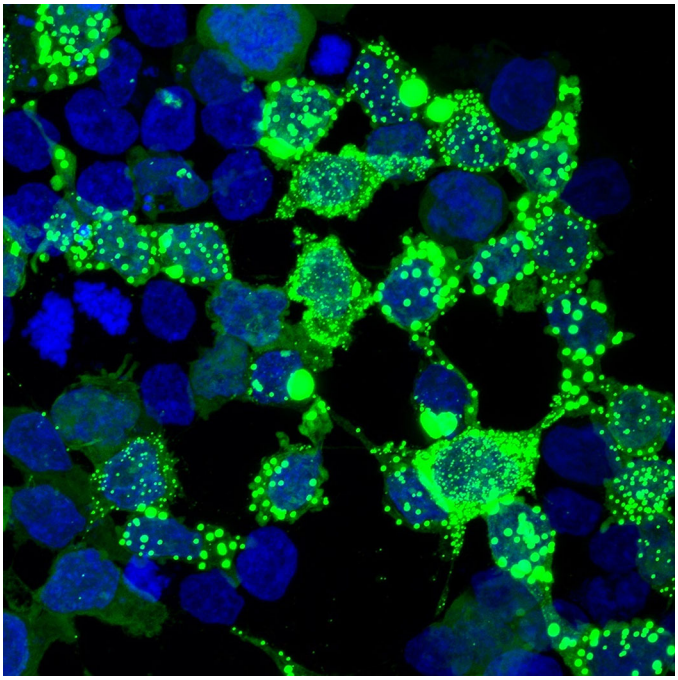
First person – Rebecca San Gil

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. Rebecca San Gil is first author on 'Neurodegenerative disease-associated protein aggregates are poor inducers of the heat shock response in neuronal cells', published in JCS. Rebecca conducted the research described in this article while a PhD student in Heath Ecroyd's lab at the Illawarra Health and Medical Research Institute, University of Wollongong, Australia. She is now a Fight MND Early Career Research Fellow in the lab of Adam K. Walker at the Queensland Brain Institute, The University of Queensland, Brisbane, Australia, investigating the cell and molecular processes that regulate protein aggregation and enhance neuronal survival in neurodegenerative diseases.

Rebecca San Gil

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

Have you ever slept through your alarm in the morning? Sometimes, cells can sleep through their warning alarms as well. Usually, when proteins in the cell become unstable and misfold, this acts as an alarm to trigger a protein quality control pathway called the heat shock response. In this work, we show that unstable proteins involved in neurodegenerative diseases fail to trigger a heat shock response. As a consequence, we hypothesise that this leads to the formation of toxic protein tangles, called inclusions, and subsequent neuronal death in neurodegenerative diseases.



An extremely aggregation-prone mutant of TDP-43 expressed in cells forms thousands of bright inclusions.

Rebecca San Gil's contact details: Neurodegeneration Pathobiology Laboratory, Queensland Brain Institute, The University of Queensland, Building 79, Upland Road, Brisbane, Qld 4072, Australia.
E-mail: r.sangil@uq.edu.au

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

An IncuCyte Zoom live-cell imaging system was installed at my institute at a very opportune time in my PhD research and helped me to realise the full potential of the heat shock response reporter cell line I had developed for this work. I had been conducting endpoint experiments, including flow cytometry and immunoblotting to detect the induction of the heat shock response; however, with the IncuCyte, I was able to visualise for the first time the kinetics and magnitude of the heat shock response in the reporter cells in real time. This was a very exciting 'eureka' moment for me as a PhD student.

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

I thought this work would be a great fit for the readership of the journal because it provides insight into the role of the heat shock response in protein aggregation associated with Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis. In addition, The Company of Biologists is very supportive of early-career researchers and supported me during my PhD on a research exchange to University College London, which was an excellent experience.

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

I have had many mentors throughout my research career who have been extremely generous with their time and advice. I have always sought advice on certain things from multiple people, because their experiences and perspectives are varied, and this has always given me greater insight into how to solve a problem or make a big decision.

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Sometimes I would get conflicting advice from two different mentors, for example, 'your thesis doesn't get written at the bar' and 'the best collaborations are struck at the bar'. By listening to both mentors, I was able to write my thesis in a timely manner but also grow excellent friendships and collaborations that continue today. The guidance I have received is special because I have asked and listened to a network of mentors who have given me their valuable time.

What's next for you?

I have very recently started a Fight MND Early Career Research Fellowship at the Queensland Brain Institute, where I am using genome-wide CRISPR screens to identify genes and proteins involved in motor neuron disease-associated protein aggregation. I am very motivated to begin this project and determined to identify some new therapeutic targets for this devastating disease.

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

I love travelling and cooking and, since it comes with the territory of being a researcher, the holidays are thoroughly researched and the recipes undergo a number of independent repeats before publication.

Reference

San Gil, R., Cox, D., McAlary, L., Berg, T., Walker, A. K., Yerbury, J. J., Ooi, L. and Ecroyd, H. (2020). Neurodegenerative disease-associated protein aggregates are poor inducers of the heat shock response in neuronal cells. *J. Cell Sci.* **133**, jcs243709. doi:10.1242/jcs.243709