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FIRST PERSON

First person – Oluwaseun Akinyele

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. Oluwaseun Akinyele is first author on 'Impaired polyamine metabolism causes behavioral and neuroanatomical defects in a mouse model of Snyder–Robinson syndrome', published in DMM. Oluwaseun is a postdoc in the lab of Dwi U. Kemaladewi at the University of Pittsburgh School of Medicine, investigating how polyamine perturbation causes a range of human diseases, from breast cancer to rare neurological disorders, such as Snyder–Robinson syndrome.

Oluwaseun Akinyele

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

Snyder–Robinson syndrome (SRS) is a rare neurological disease with no available treatment. Development of treatments for SRS is hampered by the lack of a suitable preclinical animal model in which to study the disease and evaluate any potential treatment. In this study, we studied SRS disease presentation in a recently generated mouse model called the G56S mouse. We investigated possible behavioral and anatomical defects as well as altered cellular and molecular processes that might be contributing to the manifestation of the disease. We observed that the G56S mice exhibited abnormal behavioral responses, such as decreased activity and elevated fear responses, and brain imaging showed decreased total and regional brain volumes. Furthermore, our results suggest that abnormal respiration in mitochondria (the powerhouse of the cell) could be a contributor to the disease pathogenesis.

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

The results presented in this study will enhance our understanding of SRS and provide useful parameters that may be adopted in efforts to assess the efficacy of any therapeutic agents and/or improve the current clinical management of the disease.

G56S mouse is the first preclinical murine model of Snyder–Robinson syndrome that mimics the type of gene variant found in some patients.

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

One of the main advantages of the experimental system used in this study is that the G56S mouse is the first preclinical murine model of SRS that mimics the type of gene variant found in some patients. This model, as presented in this study, will help us gain a better understanding of SRS disease pathogenesis to help improve the current clinical management of the disease. Also, this mouse model will serve as a useful tool to develop and evaluate possible therapeutic interventions for the disease. The main drawback of using this animal model is the length of time it takes to generate enough mice to complete some of the assays described in this study. SRS is an X-linked disease and, as such, only males are affected. However, affected male mice, particularly on the C57BL/6J genetic background used in this study, are generated at a rate below the expected Mendelian ratio. This, to a large extent, increased the time taken to complete some of the experiments described in this study. However, this limitation has largely been overcome by the transfer of the disease-causing mutation to another mouse of a different genetic background, B6C3H, which is a mix of the C57BL/6J and C3H/HeJ backgrounds. So far, this new mouse strain appears to have improved breeding and, thus, the number of G56S mutant male mice available for experimental assays has been increased.

What has surprised you the most while conducting your research?

The one thing that has surprised me the most since the start of my current research is the amount of support that I have received from both within and outside of the University of Pittsburgh. Coming from a research background in cancer, with no prior research experience in genetics and genetic diseases, I was initially nervous as to how I would cope with moving to a different country, settling into a different environment, and undergoing research that was (then) completely outside of my expertise. However, the kind of support that I have received from my research mentor, Dr Dwi Kemaladewi, other members of the research group, and the staff of

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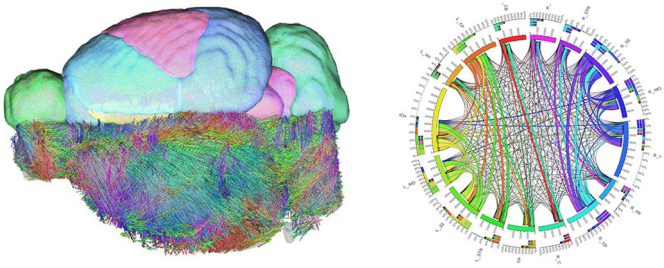
If we don't study it, no one will!



Whole ex vivo mouse brain fiber tract. We delineated the brain network architecture underlying the neurological deficits with high-definition magnetic resonance imaging (MRI) diffusion tractography, followed by topological analysis with graph theory. The image on the left represents the neuronal white matter tracks of the mouse brain by high-resolution MRI diffusion tractography and atlas-based segmentation of brain regions, and the image on the right is a representative connectogram to evaluate how brain regions are connected and organized. Analysis of the diffusion tractography and connectogram will enable us to better understand the brain network organization underlying some neurological diseases, such as Snyder–Robinson syndrome.

other research facilities has been exceptional. In addition, I have had the opportunity of collaborating with other researchers from outside of the University of Pittsburgh and the amount of support I have received so far has been very impressive.

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?

One of the main challenges impacting my research at this time is the limited funding opportunities available to young scientists like me. This funding limitation is further compounded by the immigration status of scientists, as young foreign scientists doing their research in this country (USA) are limited in the number of government-funded research grants they are eligible to apply for. Over the next 10 years, there is a need for more research funding, especially for young/junior scientists, by both government and private organizations. Also, academic/research institutions need to create funding opportunities that only their trainees can apply to, irrespective of their nationality. This will go a long way in enhancing the trainees' career development and thus serve as a springboard to apply to national and international funding opportunities.

It is my belief that science should be done in a fairer and more equitable environment that promotes equal opportunities and fosters inclusiveness for all scientists irrespective of their background, race or color.

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

As mentioned earlier, there is a need for more funding for research as scientists often face fierce competition for limited grants. Also, many of the application processes for the available grants are somewhat cumbersome and thus need to be better streamlined for easy and successful application processes. In addition to funding, there is a need to make research more openly accessible. Although there has been an increase in the number of open-access journals in the last few years, the expansion of this initiative would promote wider dissemination and sharing of scientific knowledge and build more collaboration among scientists. Finally, we live in a society with lots of systemic issues, such as racial discrimination, conscious and unconscious biases, prejudice etc., and the scientific community is not immune to these societal problems. Thus, academic, research and government institutions need to come up with measures to identify and address these issues within the scientific community. It is my belief that science should be done in a fairer and more equitable environment that promotes equal opportunities and fosters inclusiveness for all scientists irrespective of their background, race or color. These changes and many more will go a long way in improving the professional lives of many scientists.

What's next for you?

I plan to continue working on Snyder–Robinson syndrome. My team and I are moving on to the phase of our study on SRS that involves developing and evaluating gene therapy as an effective therapeutic approach for the disease using the G56S mouse model.

Reference

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