

FIRST PERSON

First person – Cameron Johnstone

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. Cameron Johnstone is first author on 'Functional and genomic characterisation of a xenograft model system for the study of metastasis in triple-negative breast cancer', published in DMM. Cameron is an Honorary Fellow in the lab of Matthias Ernst at the Olivia Newton-John Cancer Research Institute, Heidelberg, Australia, investigating aspects of triple-negative breast cancer including characterisation of cancer subtypes, identification of new targets for therapy, molecular mechanisms of metastasis and development of imageable xenograft and allograft mouse models.

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

The research provides deep characterisation of several variants of a commonly used breast cancer cell line MDA-MB-231, and these will be available to the research community to use. The work identifies potential new players in metastatic dissemination and also new targets for therapy. The next step is to define which of the genes identified are genuinely good targets to go after in targeted therapy.

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

The advantages are firstly that the experimental system is isogenic, that is all cell lines were derived from the same original tumour, but they behave completely differently in experimental mice. So the differences in metastasis cannot be due to germline genetic variation. Secondly, because the lines are human, targeted therapies against human antigens and enzymes can be used. The obvious drawback is that in order to engraft human tumour cells, the host mice have defective adaptive and innate immunity. However, the genes identified in this study can now be functionally tested in both the described xenograft system and also in immunocompetent allograft models of metastatic breast cancer. But as an initial screening step, many genes could be tested in a medium-throughput assay such as the chick chorioallantoic membrane (CAM) assay.

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Cameron Johnstone

What has surprised you the most while conducting your research?

One thing would be how labour-intensive mouse experimentation is. Both in terms of generating data over what can be several months and then analysing the acquired data. This is on top of animal ethics, animal welfare and regulatory requirements.

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

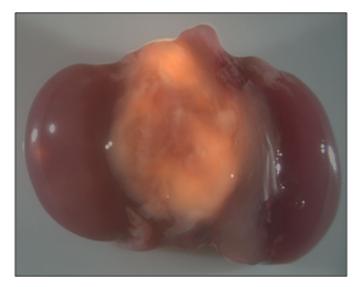
The most difficult challenge is making cancer research sustainable. This will be aided by exploring all avenues including partnering with the community, with patients and their advocates, and with the private sector as well as local, state and federal governments.

In terms of breast cancer, one big problem is that no two tumours are the same, so heterogeneity is an issue. Applying combinations of targeted therapies will be important, as well as immunotherapy and treatments directed to the elusive cancer stem cell population.

"[...] big problems arise at the mid-career level if you are unable to, or don't want to, run your own laboratory."

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

I think the professional lives of early-career scientists are reasonably okay, although the pay is not high enough in countries like the US. However, big problems arise at the mid-



Merged brightfield and fluorescent (tdTomato) image of a spontaneous metastasis formed between the kidneys in a mouse inoculated with tagged MDA-MB-231_HM triple-negative breast cancer cells.

career level if you are unable to, or don't want to, run your own laboratory. This is because paid jobs are scarce at this level, especially ones with more than a year of security. One potential solution is to increase the number of 'staff scientist' positions in research institutions. However, this will be met with solid resistance at the institutional level because of the increased cost associated with hiring more experienced personnel. I still believe doing a PhD is worthwhile. However, individuals need to consider very carefully whether they really need to take a postdoc position. In many (most) instances, people will be better served moving directly into the private sector. Once on this merry-go-round for a while, it is very hard to jump off.

What's next for you?

To regain employment in a cancer research-related role in academia or the private sector or failing that, to change careers.

Reference

Johnstone, C. N., Pattison, A. D., Gorringe, K. L., Harrison, P. F., Powell, D. R., Lock, P., Baloyan, D., Ernst, M., Stewart, A. G., Beilharz, T. H. and Anderson, R. L. (2018). Functional and genomic characterisation of a xenograft model system for the study of metastasis in triple-negative breast cancer. *Dis. Model. Mech.* 11: dmm032250.