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FIRST PERSON

First person – Vanessa Chong-Morrison

First Person is a series of interviews with the first authors of a selection of papers published in Biology Open, helping researchers promote themselves alongside their papers. Vanessa Chong-Morrison is first author on 'Ac/Ds transposition for CRISPR/dCas9-SID4x epigenome modulation in zebrafish', published in BiO. Vanessa conducted the research described in this article while a D.Phil. candidate, then as a postdoc in Tatjana Sauka-Spengler's lab at Weatherall Institute of Molecular Medicine, University of Oxford. She is now a postdoc in the lab of Steve Wilson at UCL, investigating Molecular and multiomics approaches to understand how components of the genome, including but not limited to protein-coding genes, orchestrate developmental processes.

Vanessa Chong-Morrison

Describe your scientific journey and your current research focus

My first research experience was as an Amgen Scholar at LMU München. I remember unsuccessfully trying to clone one construct to test if a protein had a role in nucleosome positioning. In my final year at King's College London, I took a chance and signed up for the Mechanisms of Development module despite not having done embryology the previous year – I thought the syllabus looked interesting. That decision did not disappoint, and combined with my interest in molecular genetics, selected a research project investigating the genetic regulation of mouse skeletomuscular development. I tried to make an *in situ* probe for a putative non-coding transcript, but despite my best efforts it refused to be sufficiently amplified. This experience sowed the seed for thinking beyond protein-coding genes during development. As a result, when Tatjana advertised a D.Phil. project to explore long non-coding RNAs in neural crest development, I jumped at the chance and applied to join her lab at the Weatherall Institute in Oxford. Ultimately, we realised that these components were not well-suited to existing methods. Thus, I ended up going off on several tangents in developing genetic tools (including this paper). At the point of thesis submission, I felt mentally tired from 'doing just tools and not much biology'. I was intrigued by the phenomenon of asymmetry breaking while attending the Embryology course at Woods Hole, so I visited Steve's lab and later joined as a postdoc to work on the very interesting biological question of brain left/right asymmetry. I am currently trying to work out what a miniscule organ called the parapineal does during left/right establishment in the zebrafish brain, which is a whole different challenge altogether as we do not even know most of the protein-coding genes the parapineal expresses. As for the non-coding RNA question – it is still a work-in-progress!

"I tried to make an *in situ* probe for a putative non-coding transcript, but despite my best efforts it refused to be sufficiently amplified."

Vanessa Chong-Morrison's contact details: UCL, Gower Street, London WC1E 6BT, UK.
E-mail: v.chongmorrison@ucl.ac.uk

Who or what inspired you to become a scientist?

I grew up in Malaysia and largely exasperated my teachers for sleeping in class a lot. Back then, I treated science as any other subject to aim an A grade for, purely as a measure of 'doing well' at school. This started changing during A-level Biology when we learned the rudiments of molecular biology and how genes work – I was fascinated by the genetic code, and how it underpins the tree of life. It was my first taste of learning a topic because I wanted to, and not just because I had to. I decided to pursue a BSc at university, where I particularly enjoyed tutorials conducted to dissect the lecture content beyond what was taught. Sometime in the middle of my studies I casually mentioned the thought of 'doing scientific research' to my tutor (Brian Sutton), who I owe a lot to for starting along that path. Together with two other tutors (Alison Snape and Baljinder Mankoo), they facilitated my then-evolving plans of pursuing scientific research with constant encouragement, supporting applications to undergraduate summer research programmes, as well as doctoral studentship applications (including several unsuccessful attempts).

How would you explain the main finding of your paper?

We built a toolkit that enabled tuning instead of modifying genes. This is especially useful when trying to understand how defined regions

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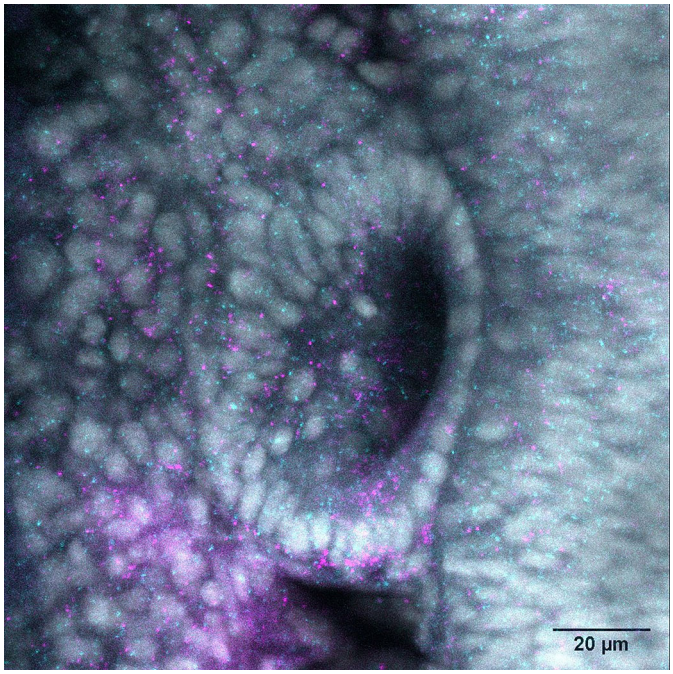

A close-up of the developing ear (otic vesicle) in the zebrafish with non-coding antisense (cyan) and protein-coding sense (magenta) sox9a transcripts stained as coloured puncta. Nuclei visualised as grey spheres.

within DNA work, but editing them e.g. by introducing mutations is not an option from a scientific and/or logistical perspective.

"We built a toolkit that enabled tuning instead of modifying genes."

What are the potential implications of this finding for your field of research?

By presenting this toolkit to the community, we hope to provide an approach that is cost-effective and flexible to researchers' needs. It was a turning point for us when we realised the method was not reliant on germline transmission for interpretable experimental results. This means that exploratory (and often, preliminary) experiments are achievable without excessive financial and/or animal cost, thus also aligning with the 3Rs (Replacement, Reduction and Refinement) framework for animal research.

Emelyanov et al. 2006 first showed that maize Ac/Ds transposition works in an animal i.e. the zebrafish; we expanded on this and showed that its utility can be appreciated without making transgenics. Together, these results hint at Ac/Ds's potential application in non-genetically tractable organisms to dissect genes and genome function.

Which part of this research project was the most rewarding?

Observing, for the first time, live embryos injected with a *pax3a* enhancer cloned into our Ac/Ds construct. Upeka (one of the co-authors – she was a postdoc while I was a graduate student) and I had tried several iterations of the construct backbone with incremental success. To finally see healthy F0 injected embryos underneath a fluorescent stereomicroscope with beautiful, clean, and most importantly – consistent - tissue-specific labelling … that was something! This started the ball rolling and the next thing we knew every fish person in the lab was enthusiastically cloning and screening putative enhancers from their genome-wide data. We now have a catalogue of enhancers for different developmental biology questions, and a handful have led to papers/preprints (Weinberger et al. 2020, 2021; Lukoseviciute et al. 2018, 2021). It is a privilege to participate in lab meetings and learn how others have adapted the toolkit for their own questions. In many ways, the paper itself is secondary to its journey - it boasts no novel finding(s) per se, but its lengthy evolution did bookmark a period of major life changes exacerbated by Covid. The unwavering support from both my PIs and colleagues through the years is a huge reward on its own.

What do you enjoy most about being an early-career researcher?

Having accumulated sufficient negative results by now, I enjoy being better at learning from my experiments when they do not work as intended. I think being an early-career postdoc means you have been reprogrammed to not expect successful experiments, which allows one to absorb experimental lessons with a more positive attitude. As a result, any small success is a very pleasant surprise.

What piece of advice would you give to the next generation of researchers?

I do not think this is restricted to being a researcher but explore and do what interests you.

What's next for you?

What is current are the on-going projects from my DPhil (non-coding genome) and postdoc (brain left/right asymmetry). I will then figure out what is next!

Final thoughts?

My partner and I adopted a rescue cat back in 2014. We were in the early days of implementing CRISPR protocols in the Sauka-Spengler lab, and it was all we talked about in lab meetings, so I thought why not call the cat Crispr (we did, even though my partner is not a biologist). It is remarkable to reflect how the novelty of answering 'what is your cat called' to non-biologists wearing off through the years. We used to be caught on the spot trying to explain CRISPR in lay terms, but now most do not even bat an eyelid. I think it illustrates on a tiny scale how far genome engineering and CRISPR has developed within the public's awareness.

Reference

Chong-Morrison, V., Mayes, S., Simões, F. C., Senanayake, U., Carroll, D. S., Riley, P. R., Wilson, S. W. and Sauka-Spengler, T. (2023). Ac/Ds transposition for CRISPR/dCas9-SID4x epigenome modulation in zebrafish. *Biol. Open.* **12**, bio.059995. doi:10.1242/bio.059995