Serendipity and sequencing

Dr Bryony Thompson helps doctors and genetic counsellors bring a little more certainty to patients on the receiving end of genetic testing ...

DR Bryony Thompson is an adult genomics curation scientist, and she's loving every minute of it.

Based in the Department of Pathology at the University of Melbourne and working with Professor Ingrid Winship's Adult Clinical Genetics group, Dr Thompson plays daily in the wonderland that is variants of uncertain significance.

"It's my dream job," she tells the *MJA*.

When a patient is tested for genetic causes of their particular cancer, a raft of results come back from the lab. Sometimes it is clear that a particular genetic variant is the cause of the disease. Sometimes it is clear that it is not.

And then there are the variants of uncertain significance (VUS).

"They are the bane of doctors' and genetic counsellors' existence," says Dr Thompson, "because they have to explain to patients what has been found.

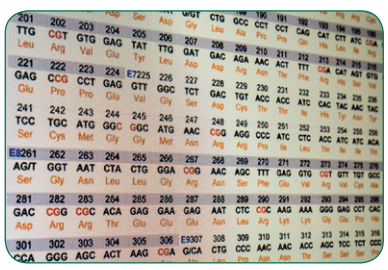
"Some doctors don't quite understand VUS and then treat it as a significant result when it should not be."

And that's where Dr Thompson's job begins.

"Part of my job is to pull information from all these different databases, and my own expertise, to try and make more sense of that variance," she says. "Luckily there are computer programs that pull all the information together."

Sometimes, she says, results can come back from laboratories across the country and around the world, and they can be "a little vague".

"That's where I come in. I've already had a few queries from the genetic counsellors. They had some testing from other labs in the US and the test reports [were] a little bit vague, so they asked me to look at them.



"I pulled out some more information from other databases and in one difficult case I was able to say that [the variant found] probably was not the cause of the disorder because it was based on conservation in primates."

It's no surprise that Dr Thompson started off in forensics. She was part of the first cohort to go through Griffith University's Bachelor of Forensic Science degree, graduating in 2006.

"I was a big fan of the X-Files," she says.

"[The course] teaches a really good basis in science because you learn about all the medico-legal stuff and so you learn how to do good science.

"But I realised that there weren't too many jobs in forensics that wouldn't involve joining the police force, which wasn't my idea of a good time."

She opted for an honours year, working in a lab at the Queensland Institute of Medical Research, and was offered a job as a research assistant with Associate Professor Amanda Spurdle. That led to a PhD on variants of uncertain significance from the University of Queensland, working in collaboration with the International Society of Gastrointestinal Hereditary Tumours (InSIGHT), and an early career fellowship from the NHMRC which took her to the Huntsman Cancer Institute at the University of Utah in the US.

Dr Thompson's specific expertise is with mismatched repair genes, specifically the ones associated with Lynch syndrome, the hereditary susceptibility of colorectal and endometrial cancers "and a bunch of other cancers".

During her time with InSIGHT she helped develop classification criteria which were specific for mismatched repair genes and helped inform guidelines from the American College of Medical Genetics which allow curators like Dr Thompson to drill down into a much wider set of genes and disorders.

Dr Bryony Thompson

Earlier this year Dr Thompson came back from Utah to complete her fellowship at the University of Melbourne. Three days later Professor Winship invited her for a cup of coffee.

"The [Royal Melbourne] wants to start doing whole exome sequencing for some cases that are a bit difficult to figure out and look like they may have a genetic cause for their disorders or disease," says Dr Thompson.

"At the moment they just send it out to different labs around the country or around the world.

"Ingrid found some money so now part of that process is trying to curate the genomes to figure out what we can find in the exome sequencing that may be causing that particular phenotype."

It was another example of being in the right place at the right time, she says.

"I dropped my fellowship because this is my dream job. I'd love to do this for a long time.

"I had wanted to get out of academia and get into the more diagnostic, lab-based work, so the timing was perfect. I'm really excited about this opportunity."

How would she recommend this job to upcoming students?

"It's a job where you'll have a lot of variety," says Dr Thompson.

"Because the cases that will go up for whole exome sequencing are the difficult cases where there is possibly no defined set of genes [causing phenotypes] you really have to look at all of them.

"There is so much variety, and it's all challenging, but it's going to be exciting."

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Cate Swannell

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