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Want to Work on Asthma Genetics?

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Abstract

Twins, data and emails. Some of the words that first come to mind when I think of Nick. Lots of twins. With lots of data. And short single-finger-typed emails. And great wine. Well, it works, there is no doubt. That's how I ended up in Australia, working on asthma genetics.

Keywords: Asthma; genetics; Nick Martin

It's September 11, 2001, and I have just landed in Brisbane. Why? Because of Nick. Well, and a few other reasons, but mostly because of Nick. A year or so earlier, fresh from finishing my Biology degree in Lisbon, I sat at my computer wondering where — and in what field — to do a PhD. A lot of excitement around the future of human genetics then, so that seemed like a better career move than birdwatching. And Australia seemed exotic enough, with Brisbane just in the right spot. So I googled 'genetics Brisbane', easy. Sure enough, first hit was Genepi at the Queensland Institute of Medical Research (QIMR). Nick's picture, some list of papers and an email address. Dear Nick — I'm pretty sure I'm going to get a PhD scholarship from the Portuguese Government. I'm keen on genetics and maybe something related to the immune system. I see you work in this area. Will you take me on as your PhD student? Something along those lines. In typical Nick style, literally a couple of hours later, I get a reply: sure, you cocky Portuguese bastard. Want to work on asthma genetics? And that was it. The first and only email I sent to find a PhD. Twenty years and three Australian children later, here we are. My life would have been totally different had Nick not taken a chance on me.

Okay, a little bit on asthma genetics. Again, Nick's fingerprints are all over it. It is now October 2001. I have got this great study for you: 3073 twins and their families, with an asthma proband and lots of questionnaire and clinical data. A goldmine! Just get your hands dirty and start analyzing the bloody data. Of course, learn a bit of Mx first. Yaikes. Well, weren't you in for a treat, hey Nick? Six months later, and not one single table with results.

In fact, I am just getting warmed up in my thorough (Nick: exasperating) review of asthma biology, linkage analysis and whatever else I thought I needed to know first. It was probably September 2002 when Nick finally got some p values from me. Apparently, he was so worried that he considered pulling the plug. Confirm or deny?

But data analysis I eventually did, with brilliant supervision from both Nick and David Duffy. And the Sequana dataset was indeed a goldmine for me. We analyzed it in every possible way, and in doing so I got my training in asthma genetics. Did we make any significant discoveries in this era of linkage analysis? Probably not. Yes, we found some linkage peaks, but the odds are none of them reflected an underlying true asthma risk locus. I guess we will never know. But we did learn a lot. And in a heartbeat, 2005 was upon us — single-nucleotide polymorphisms, no more microsatellites!

It did take a few more years, but eventually the genetics of asthma succumbed to the new technology, collaborative spirit and ever increasing N. First it was *ORMDL3*, completely out of the blue, then another 30 loci by the end of 2016. We helped find *IL6R* and a few other loci, which would not have happened without the thousands of DNA samples that Nick collected throughout the years. We are now probably close to 200 risk loci for asthma. Have these discoveries made any difference? I think they absolutely are making a difference. It would be very naive nowadays to ignore evidence from human genetics when making decisions about which targets to pursuit for clinical development. Where will we be when Nick retires? Wait. Will Nick ever retire?