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Article

It's in the Bloody Genes!

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Abstract

Blood cell concentrations for most cell types are highly heritable. Data from Nick Martin's twin registry provided much of the data for the early heritability and linkage studies of blood cell related traits and have contributed significantly to more recent genomewide association studies that have successfully identified individual genetic loci.

Keywords: Nick Martin; twin; genomewide association study; linkage; blood cells

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I first heard about Nick Martin in 1998. I had come to his laboratory to have lunch with my former honors supervisor, Dr Margie Wright, who had recently moved from the University of Queensland Psychology Department to work in Nick's group at the Queensland Institute of Medical Research. I remember asking her what she was working on, and seeing some complicated looking figures (path diagrams) and equations (Linear Structural Relations (LISREL) notation) in a thick white book (Neale & Cardon, 1992). Although I had literally done no genetics at university, I remember thinking that the combination of statistics and biology looked interesting and might suit me.

A few weeks later I was back to meet Nick for the first time to discuss the possibility of doing a PhD in his laboratory. I was working as a medical representative for a pharmaceutical company at the time, having left university temporarily after a particularly hectic honors year, and wanted to earn some money for a while and do something outside of academia. 'God! Why the hell are you doing that?' Nick asked me in what I would soon come to recognize as classic Martin fashion, when I first met him. 'Why don't you go and work on an oil rig off the coast for a year?' Apparently, he also later commented to Margie about how I seemed nice enough, but wasn't a massive fan of my baseball cap (which he swore black and blue lowered the IQ of the wearer by at least 10 points). Despite his reservations over my choice of fashion, Nick accepted me into his laboratory shortly thereafter, in what would later turn out to be a major turning point in my life — although sadly for both of us, not my wardrobe ...

The PhD project I chose was a genetic study of blood cell concentrations in Nick's adolescent twin cohort. Unbeknownst to me at the time, many years previously Nick had had a meeting with Ian Frazer, the inventor of the Gardasil vaccine for human papilloma virus and cervical cancer (back then it would still be some years before the vaccine had Food and Drug Administration (FDA) approval and Ian attained scientific superstar status). Nick had had the incredible foresight to make sure that the blood samples taken from the twins were sent over to Ian at the Princess Alexandra Hospital (where incidentally I am now based) for a full blood count and lymphocyte subsets analysis. The result was the largest genetically informative dataset of blood cell measures in the world at that time.

The maiden paper from my PhD was the first large-scale study of the heritability of blood cell counts (Evans et al., 1999). In it, we showed that the concentration of most blood cells was highly heritable, despite the considerable inter-individual and circadian variation that characterized such measures. The heritability study was published in *Twin Research*, and strangely enough, even though the field has moved on, it is still one of the most cited papers in its area — although perhaps not for the reasons we expected. The main reason in fact is that apparently the manuscript has become a teaching aid for many aspiring students of behavior genetics who wish to use the classical twin study to conduct heritability analyses. Buried within its pages is a description of the procedure for testing the equality of means, variances and covariances across the different sexes, birth orders and zygosities — which Nick dutifully drummed into my head during the first few months of my PhD. The paper is used as a teaching aid at the introductory Boulder Workshop and apparently at others around the world also. Indeed, the paper always gets a citation bounce every alternate year because of its regular appearance (I have christened this effect on citation counts the 'Medland Effect').

In 2004, we published the first linkage studies of blood cell traits, including one of the first papers to use multivariate quantitative trait locus (QTL) linkage analysis in order to detect complex trait loci (Evans, Zhu, Duffy, Frazer et al., 2004; Evans, Zhu, Duffy, Montgomery et al., 2004a, 2004b), and several years later genomewide association meta-analyses (Ferreira et al., 2009, 2010; Gieger et al., 2011; van der Harst, 2012) — although by this time I had long left the laboratory and Manuel Ferreira and others had taken over the lead on this work. It always makes me smile that these later papers have made it into some of the most prestigious scientific journals (*Cell*, *Nature*, *American Journal of Human Genetics*), yet I remember very clearly an incident from a Cooperative Research Centres conference where a senior Australian academic (who I will not name) got up and after a tirade of 3 min tried to skewer me, a

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fresh-faced second-year PhD student, about what the point was in analyzing the genetics of blood cells, because we 'knew everything about them already' and I was wasting my and everyone else's time.

Needless to say, Nick disagreed — and quite clearly so did *Cell*, *Nature* and many other top-tier journals as it turned out.

Happy 70th birthday Nick. Thanks for your generosity and for being a supportive supervisor and mentor. I look forward to collaborating with you for many years to come.

References

Evans, D.M., Frazer, I. H., & Martin, N. G. (1999). Genetic and environmental causes of variation in basal levels of blood cells. *Twin Research*, *2*, 250–257.

Evans, D. M., Zhu, G., Duffy, D. L., Frazer, I. H., Montgomery, G. W., & Martin N. G. (2004). A major quantitative trait locus for CD4-CD8 ratio is located on chromosome 11. *Genes & Immunity*, *5*, 548–552.

Evans, D. M., Zhu, G., Duffy, D. L., Montgomery, G. W., Frazer, I. H., & Martin N. G. (2004a). Major quantitative trait locus for eosinophil count is located on chromosome 2q. *Journal of Allergy and Clinical Immunology*, *114*, 826–830.

Evans, D. M., Zhu, G., Duffy, D. L., Montgomery, G. W., Frazer, I. H., & Martin N. G. (2004b). Multivariate QTL linkage analysis suggests a QTL for platelet count on chromosome 19q. *European Journal of Human Genetics*, *12*, 835–842.

Ferreira, M. A., Hottenga, J. J., Warrington, N. M., Medland, S. E., Willemsen, G., Lawrence, R. W., Boomsma, D. I. (2009). Sequence variants in three loci influence monocyte counts and erythrocyte volume. *American Journal of Human Genetics*, *85*, 745–749.

Ferreira, M. A., Mangino, M., Brumme, C. J., Zhao, Z. Z., Medland, S. E., Wright, M. J., Martin, N. G. (2010). Quantitative trait loci for CD4:CD8 lymphocyte ratio are associated with risk of type 1 diabetes and HIV-1 immune control. American Journal of Human Genetics, 866, 88–92.

Gieger, C., Radhakrishnan, A., Cvejic, A., Tang, W., Porcu, E., Pistis, G., Soranzo, N. (2011). New gene functions in megakaryopoiesis and platelet formation. *Nature*, *480*, 201–208.

Neale, M., & Cardon, L. R. (1992). *Methodology for genetic studies of twins and families*. Springer Science & Business Media.

van der Harst, P., Zhang, W., Mateo Leach, I., Rendon, A., Verweij, N., Sehmi, J., Chambers, J. C. (2012). Seventy-five genetic loci influencing the human red blood cell. *Nature*, *492*, 369–375.

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