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Exploring host-immune-microbial interactions during intestinal schistosomiasis

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Curriculum vitae

Alice Harriet Costain was born on the 2nd of March 1994 on the Isle of Man (British Isle). She completed her primary and secondary education on the island, before moving to the UK, where she undertook a Bachelor of Science (Bsc Hons) in Physiology at the University of Manchester (2015). Whilst studying for her Bsc, Alice developed a strong enthusiasm towards the immune system and parasitic worms, with a particular admiration towards *Schistosoma* blood flukes. Driven by her fascination in immunology, Alice enrolled for an MSc in Integrated Immunology at the University of Oxford (2016). Here, Alice completed an intestinally focused research project, was introduced to the fascinating concept of Regulatory B cells (Bregs) and her excitement towards parasites grew stronger. Combining her love for worms and mucosal immunology, Alice applied for an internship with Prof Hermelijn Smits (2016; LUMC; Boehringer Ingelheim funded), where she began investigating the link between schistosome infections, leaky guts and Breg generation. This 6 month internship soon transpired into a collaborative PhD project between Leiden University and the University of Manchester, under the supervision of Prof Hermelijn Smits and Prof Andrew MacDonald (starting April 2017). During the writing of this thesis, Alice was offered a post-doctoral position with Prof Andrew MacDonald, where she continues to explore the enigmatic process of schistosome egg migration, and its impact on barrier integrity, host immunology and the local microbiota.

List of publications

1. **Alice H. Costain**, Alexander T. Phythian-Adams, Stefano A.P. Colombo, Angela K. Marley, Christian Owusu, Peter C. Cook, Sheila L. Brown, Lauren M. Webb, Rachel J. Lundie, Hermelijn H. Smits, Matthew Berriman and Andrew S. MacDonald (2022). *Dynamics of host immune response development during Schistosoma mansoni infection*. **Frontiers in Immunology**, 13:906338
2. Lauren M. Webb, Alexander T. Phythian-Adams, **Alice H. Costain**, Sheila L. Brown, Rachel J. Lundie, Peter C. Cook, Lucy H. Jackson-Jones, Angela K. Marley, Hermelijn H. Smits, Elia D. Tait Wojno and Andrew S. MacDonald. (2021). *Plasmacytoid dendritic cells facilitate T helper cell cytokine responses throughout Schistosoma mansoni infection*. **Immunohorizons**, 5, 721-732.
3. Emma L. Houlder, **Alice H. Costain**, Peter C. Cook and Andrew S. MacDonald (2021). *Schistosomes in the Lung: Immunobiology and Opportunity*. **Frontiers in Immunology**, 12:635513
4. Alba Cortés, Simon Clare, **Alice H. Costain**, Alexandre Almeida, Catherine McCarthy, Katherine Harcourt, Cordelia Brandt, Charlotte Tolley, James Rooney, Matthew Berriman, Trevor Lawley, Andrew S. MacDonald, Gabriel Rinaldi and Cinzia Cantacessi (2020). *Baseline Gut Microbiota Composition Is Associated With Schistosoma mansoni Infection Burden in Rodent Models*. **Frontiers in Immunology**, 11:593838
5. Saeed Katiraei, Margreet R. de Vries, **Alice H. Costain**, Kathrin Thiem , Lisa R. Hoving Janna A. van Diepen, Hermelijn H. Smits, Kristien E. Bouter, Patrick C. N. Rensen, Paul H. A. Quax, Max Nieuwdorp, Mihai G. Netea , Willem M. de Vos , Patrice D. Cani, Clara Belzer, Ko Willems van Dijk, Jimmy F. P. Berbée, Vanessa van Harmelen (2019) *A. muciniphila exerts lipid-lowering and immunomodulatory effects without affecting neointima formation in hyperlipidemic APOE*3-Leiden.CETP mice*. **Molecular Nutrition & Food Research**, 64(15):1900732
6. Katja Obieglo, **Alice H. Costain**, Lauren M. Webb, Arifa Ozir-Fazalalikhani, Shelia L. Brown, Andrew S. MacDonald, Hermelijn H. Smits (2019). *Type I interferons provide additive signals for murine regulatory B cell induction by Schistosoma mansoni eggs*. **European Journal of Immunology**, 49(8)
7. **Alice H Costain**, Andrew S. MacDonald and Hermelijn H Smits (2018), *Schistosome Egg Migration: Mechanisms, Pathogenesis and Host Immune Responses*. **Frontiers in Immunology**, 10
8. Grigory Ryzhakov, Nathaniel R. West, Fanny Franchini, Simon Clare, Nicholas E. Iltott, Stephen N. Sansom, Samuel J. Bullers, Claire Pearson, **Alice H. Costain**, Alun Vaughan-Jackson, Jeremy A. Goettel, Joerg Ermann, Bruce H. Horwitz, Ludovico Buti, Xin Lu, Subhankar

Mukhopadhyay, Scott B. Snapper and Fiona Powrie (2018). *Alpha kinase 1 controls intestinal inflammation by suppressing the IL-12/Th1 axis.* **Nature Communications**, 9 (3797)

Contributions

Prof Hermelijn Smits and Prof Andrew MacDonald were involved in the planning and critical analysis of all thesis chapters and pushed for the publications of Chapter 2, 3 and 5.

Many members of the Smits Lab, MacDonald Lab, and Leiden Immunoparasitology group contributed to the experimental work in this thesis (i.e mouse monitoring and tissue processing) and provided invaluable discussion. In particular, Arifa Ozir-Fazalalikhan, Frank Otto, Dr Emma Houlder and Dr Stefano Colombo helped perform many schistosome infections, schistosome egg injections and faecal transplants.

Dr Alba Cortes, Dr Stefano Colombo and Dr Cinzia Cantacessi helped acquire and analyse the 16s sequencing of intestinal content in Chapter 4 and contributed to the planning of this chapter alongside Dr Gabriel Rinaldi.

Dr Melissa Lawson, Vicky Taylor, Hayley Jenkins and Paul Smith helped coordinate all GF experiments and provided great technical support and advice.

Dr Gordano Panic and Prof Jonathon Swann performed metabolomics analysis on the serum and small intestinal content samples shown in Papers 2 and 3

Dr Tovah Shaw helped with optimising schistosome intestinal preps.

Prof Meta Roestenberg, Dr Jacqueline Janse and Arifa Ozir-Fazalalikhan organised single-sex schistosome infections. Claudia J. de Dood performed the CAA analysis.

Dr Alexander Phythian-Adams, Sheila Brown, Dr Peter Cook, Dr Angela Marley, Dr Lauren Webb, Christian Owusu, Dr Rachel Lundie performed the experiments outlined in Chapter 3. Dr Stefano Colombo aided with data collation, data analysis, and planning of this chapter.

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My PhD journey began in Leiden, where two lovely people took me in and showed by the quirkiness of Dutch living. Pauline and Herman, thank you.

Arifa. Working with you has been splendid. Thank you for teaching me everything, being a wonderful colleague and a great friend; especially in the first couple months, where I rambled and bumbled in super quicker, unintelligible English! (Maybe I've slowed down a bit). I honestly wouldn't have made it through these last through years if I didn't have your help and guidance along the way.

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