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Patrick Lelliott, Ph.D.

Cell Biology and Immunology

Osaka University

Born in 1985 in Sydney, Australia

Studied Nanotechnology at the University of New South Wales and Advanced Medicine at Macquarie University, Sydney

FELLOWSHIP

College for Life Sciences

ARBEITSVORHABEN

Quantitative Biological Analysis of Neutrophils and Nets

Neutrophils are the most common white blood cells in the circulation. Despite this, they are relatively poorly understood. Until recently, neutrophils were thought to respond to invading pathogens in only two major ways: phagocytosis and degranulation. In 2004, a third process was discovered, the release of large web-like structures, termed neutrophil extracellular traps (NETs), that ensnare, immobilize, and destroy invading pathogens.

NETs are now known to be important for the immune defense against bacteria, viruses, parasites, and fungi. On the other hand, excessive and uncontrolled NET formation has been found to play a key role in cardiovascular disease, deep vein thrombosis, cancer metastasis, autoimmune diseases, and even death by sepsis. Understanding NET formation is therefore vital to understanding human disease.

My project will examine tens of thousands of images of individual neutrophils at different stages of artificially induced NET formation, obtained by imaging flow cytometry. For each cell, a high-magnification, high-resolution picture is available. This huge array of data requires a novel approach to data analysis. I will be attempting to apply methods such as machine learning and deep learning in order to identify groups of cells with similar characteristics and to discover new features and types of NET formation. These methods use artificial intelligence to identify distinguishing details in images that may not be noticeable to the human eye, working with principles similar to those used in facial recognition and fingerprint analysis.

If successful, this project may identify key features of NETs and allow us to gain new insights into the behavior of neutrophils, which will be important in preventing NET pathology and its associated diseases in the future.

Recommended Reading

Lelliott, P. M., M. Momota, M. S. J. Lee, E. Kuroda, N. Iijima, K. J. Ishii, and C. Coban (2019). "Rapid quantification of NETs in vitro and in whole blood samples by imaging flow cytometry." *Cytometry Part A* 95, 5: 565-578.

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Lelliott, P. M., B. J. McMorran, S. J. Foote, and G. Burgio (2015). "Erythrocytic iron deficiency enhances susceptibility to *Plasmodium chabaudi* infection in mice carrying a missense mutation in transferrin receptor 1." *Infect Immun* 83, 11: 4322-4334.

Lelliott, Patrick (Hoboken, NJ,2019)

Rapid quantification of NETs in vitro and in whole blood samples by imaging flow cytometry

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Lelliott, Patrick (Oxford,2019)

Heparin induces neutrophil elastase dependent vital and lytic NET formation

<https://kxp.k10plus.de/DB=9.663/PPNSET?PPN=1686934211>

Lelliott, Patrick (Washington, DC,2017)

Erythrocyte β spectrin can be genetically targeted to protect mice from malaria

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Erythrocytic iron deficiency enhances susceptibility to plasmodium chabaudi infection in mice carrying a missense mutation in transferrin receptor 1

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