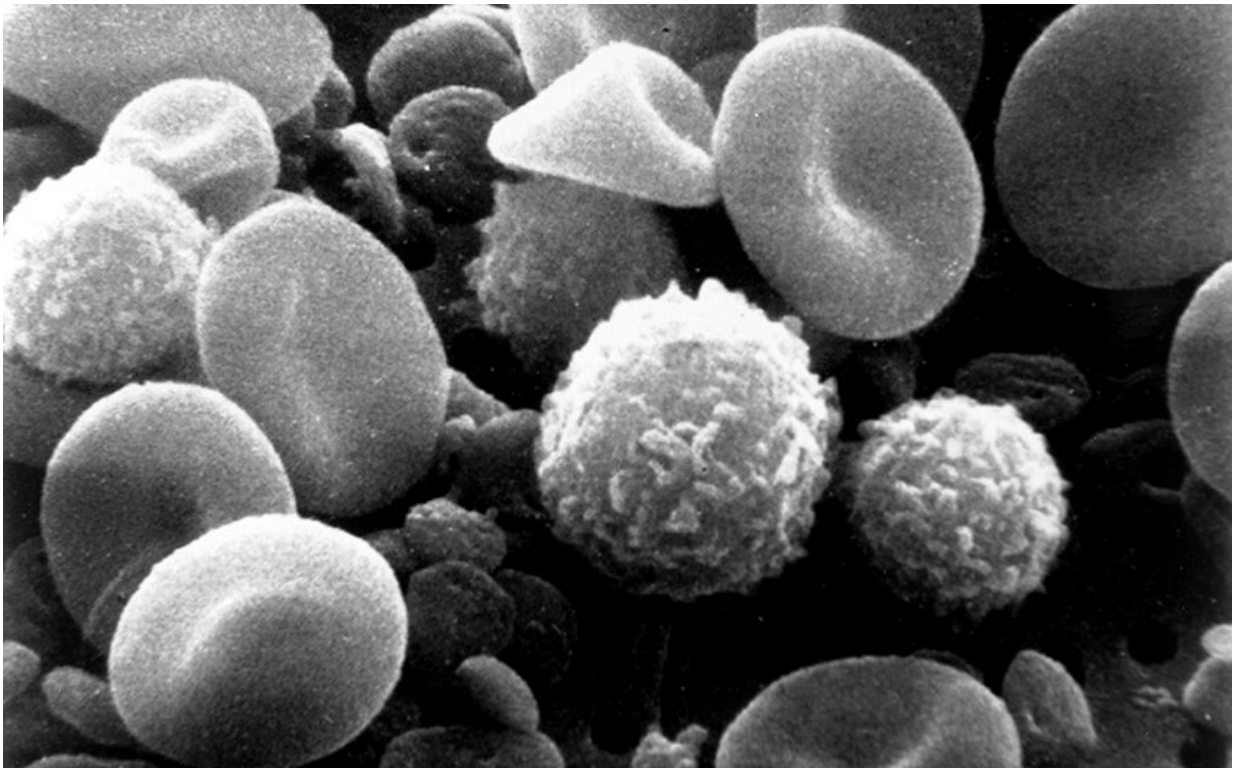
From sleeping cell to assassin—how immune cells work

October 7 2019



Myeloid immune cells alongside red blood cells in an electron micrograph of human blood. Credit: National Cancer Institute

Scientists at the University of Dundee have carried out one of the most comprehensive studies into how immune cells sense and respond to their environment to fight infection and destroy tumours.

The research team, who have published their findings in the journal *Nature Immunology*, said the results provide important insights into how immune responses might be manipulated for the treatment of autoimmune diseases and cancer.

Professor Doreen Cantrell and Professor Angus Lamond, both in the School of Life Sciences at Dundee, led the study, which focused on T lymphocytes, a population of white blood cells essential for immune responses to cancer, bacteria and viruses, and transplanted organs.

They mapped how these cells control expression of more than 9,000 proteins as they take part in immune responses. They also mapped in fine detail how an important immune-suppressive drug, used to prevent organ rejection in transplants, selectively controls these processes.

Professor Cantrell said, "These results have implications for our understanding of how harmful or beneficial immune responses can be manipulated for better health outcomes in organ transplantation and cancer.

"A critical discovery is that exposure to foreign stimuli, such as viruses and bacteria, make T lymphocytes switch on expression of key sensors for oxygen and nutrients and also make T lymphocytes switch on expression of transporters that allow cells to import nutrients from their environment.

"Drugs used to block immune responses work by controlling these key metabolic pathways."

The study also shows how the ability of immune cells to mount effective responses can be shaped by the oxygen and nutrient environment the cells work in.

The research team, including Dr. Andy Howden, Dr. Jens Huckelmann, and Alejandro Brenes, brought together experts in immunology and scientists with expertise in cutting-edge technology in mass spectrometry and data science. This allowed a unique exploration of how T cells re-programme expression of thousands of cellular proteins in response to stimulation and provided a comprehensive understanding of how immune-suppressive drugs control T lymphocyte behaviour.

Professor Lamond said, "These critical discoveries show the enormous value of the collaborative research environment here at the University of Dundee, which allows world leading scientists to bring together their overlapping areas of expertise to solve important biological problems."

The research was supported by a Wellcome Trust Strategic award to Professors Cantrell and Lamond and used equipment and facilities funded by a UK Research Partnership Investment Fund (UKRPIF) grant, awarded by Research England in partnership with the Scottish Funding Council.

More information: Quantitative analysis of T cell proteomes and environmental sensors during T cell differentiation, *Nature Immunology* (2019).
DOI: 10.1038/s41590-019-0495-x ,
nature.com/articles/s41590-019-0495-x

Provided by University of Dundee