Cell division find prompts overhaul of immune response modeling

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Research by Professor Phil Hodgkin at the Walter and Eliza Hall Institute into the mechanics of how two types of white blood cells grow and die is fundamentally changing the development of computer models that are used to predict how immune system cells respond to a pathogenic threat. Credit: Cameron Wells, Walter and Eliza Hall Institute

Research at the Walter and Eliza Hall Institute into the mechanics of how two types of white blood cells grow and die is fundamentally changing the development of computer models that are used to predict how immune system cells respond to a pathogenic threat.

A team led by Professor Phil Hodgkin, head of the institute's Immunology Division, is investigating the proliferation and survival of T and B lymphocytes - white blood cells that are crucial to the body's

ability to generate immunity.

When lymphocytes are exposed to pathogens they are stimulated to undergo a series of cell divisions, which increases the number of lymphocytes many hundredfold. After a period the cells stop dividing and 95 per cent of the newly-generated cells die.

Professor Hodgkin said although there was considerable variation in the number of divisions cells went through before they died, existing computer models had been developed assuming all cells were mechanically identical. However, biologists have long been aware that cells never behave identically. This variation is usually dismissed as 'noise' or irrelevant biological variation.

"About 10 years ago I was struck by the thought that by ignoring the immense amount of variation in cells we might be missing something important," Professor Hodgkin said. "What if the variation is a design feature of the cells? What if they're doing it deliberately? My lab has been pursuing the implications of this idea ever since."

In an attempt to revamp computer models of the immune response to accommodate individual cells, Dr Edwin Hawkins, Dr John Markham and Mr Liam McGuinness at the Walter and Eliza Hall Institute, for the first time in science, followed hundreds of lymphocytes and their offspring through all their cell divisions until their deaths. They also recorded how this variation in lymphocyte behaviour was transmitted through cell generations.

The research has been published today in the Proceedings of the National Academy of Sciences USA.

"We found that all the offspring of a single cell died at the same cell division; their lifespan is programmed from that very first cell,"

Professor Hodgkin said. "We also observed that cell 'siblings' took a similar amount of time to die. This tells us that a very large part of the fate of individual cells is locked in and programmed early."

Professor Hodgkin said it appeared that when a lymphocyte first divided chemicals were produced that were progressively diluted as the cell went through its divisions. When levels of these chemicals fell below a certain threshold the cells stopped dividing and died, he said.

"With accurate information on the time it takes for a lymphocyte to divide, the time taken to die and the number of cell divisions an individual cell goes through, we can develop new mathematical models that are correct not only at a single-cell level but that also hold true for a whole population of cells."

Accurate computer-based models of the immune response are a holy grail for scientists as they promise to unlock new therapies for infectious diseases, and allow careful investigation of autoimmune conditions.

Source: Walter and Eliza Hall Institute