MedicalXpress

Cells can influence their own destiny, research finds

January 5 2012

In a major shake-up of scientists' understanding of what determines the fate of cells, researchers at the Walter and Eliza Hall Institute have shown that cells have some control over their own destiny.

The researchers, from the institute's Immunology division, drew their conclusion after studying B cells, immune system cells that can make antibodies.

B cells can have multiple fates. Some of the more common fates are to die, divide, become an antibody-secreting cell or change what antibody they make. This all happens while the cells are proliferating in the lymph nodes.

The commonly-held view is that a cell's fate is determined by external cues such as the presence of particular hormones or cell signaling molecules.

However the Walter and Eliza Hall Institute's head of immunology, Professor Phil Hodgkin, and colleagues Dr Mark Dowling, Dr Cameron Wellard and Ms Jie Zhou, predicted that cell fates are, to a large extent, determined by internal processes.

To test their theory the research team recreated the conditions required for B cells to develop into the different cell types and then filmed the cells, working with Dr John Markham from National Information and Communications Technology Australia to develop new technology and

image analysis methods.

The research team's experimental observations were further enhanced by the expertise of mathematician Dr Ken Duffy from the Hamilton Institute, Ireland. Dr Duffy's understanding of probabilities was critical for the team to interpret the behaviour of the 2500 cells that were filmed. The team's research findings have been published today in the international journal *Science*.

Professor Hodgkin said the cells behaved as though there were internal machines that governed the cells' fates. "Each of these internal machines is like a little clock or timer for division, death, what type of antibody they make and whether they become antibody secreting cells," he said.

Dr Dowling explains it as the different fate outcomes being a competition. "Each cell will, in some sense, set up a clock that starts ticking for each of the outcomes and whatever clock goes off first is the decision that the cell makes," he said. "The cell is trying to do everything but only one fate wins."

Professor Hodgkin said even though the cells were getting the same external signals there was still considerable variation in what happened to the cell population. "A reliable proportion of the B cells would end up with each of the different fates," he said. "This suggests that external factors such as hormones or cell signaling molecules were not telling the cells what to do but were altering the probability of what the cells were going to do anyway."

When the body is responding to an infection many immune cell types, each with a different function, are produced. Dr Dowling said it could be that the body was tweaking the odds of producing particular cell types depending on the situation. "The body produces many different hormones and cell signaling proteins so the odds will be different for

different infections. A whole lot of molecules involved in the immune system will affect those odds."

Professor Hodgkin said the hope now was to create mathematical models that accurately predict how external signals will alter the probability of what an immune cell population will do. "The development of such models would help in the design of new immune therapies for autoimmune diseases and improved vaccines," he said.

Provided by Walter and Eliza Hall Institute