To Stop Or Go? How T And B Lymphocytes Regulate The Strength Of Their Response To Antigen

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Abstract
T and B-lymphocytes process affinity, co-stimulatory signals, and secreted cytokines to reach decisions about the strength and type of response to follow after challenge. By combining direct cell imaging, genetic manipulation and computer modelling we can examine cells making decisions under different stimulation combinations. Our results reveal surprisingly simple rules for cellular calculation for both classes of lymphocyte. Typically cells simply count through a series of divisions, stop and die. Varying the stimulation strength alters the proportion of cells entering the autonomous program without changing division, differentiation or survival rates. In T cells IL-2 extends the number of divisions reached in a concentration dependent manner without altering time between divisions. These results give an insight into how complex immune responses evolved from simpler pathways and suggest a signal integration calculator can be developed to dissect the influence of changes caused by drugs, or genetic polymorphisms.

Professor Hodgkin studied Microbiology at the University of Western Australia and obtained his PhD from the John Curtin School for Medical Research in Canberra in 1985. He undertook postdoctoral studies at the DNAX Research Institute in Palo Alto California where he studied the regulation of antibody production and isotype switching by B lymphocytes. In 1990 he returned to Australia to take up a Research Fellowship at the John Curtin School of Medical Research and in 1995 he was appointed Group leader at the Centenary Institute for Medical Research. In 2000 he moved again to the Walter and Eliza Hall Institute in Melbourne and in 2006 was appointed Head of the Immunology Division. He was President of the Australasian Society of Immunology (ASI) from 2005 to 2006.

Professor Hodgkin’s research interests centre upon immune regulation. In recent years he has focussed on quantitative studies of T and B cell growth and differentiation to inform development of computational models of immune cell behaviour. His laboratory has established techniques to directly image cells undergoing fate changes to inform the research and explore the impact of cytokines and genetic changes on lymphocyte growth, survival and differentiation.