

THE CHINESE UNIVERSITY OF HONG KONG SCHOOL OF LIFE SCIENCES

Cytokine-stimulated differentiation of granulocytes & macrophages: targeting microRNAs in allergic inflammation

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December 4, 2012 (Tuesday)

11:30 am

LSB_LT5, Lady Shaw Building
The Chinese University of Hong Kong

ALL ARE WELCOME

Cytokines are key messengers of the immune system and play critical roles in immune responses to infections and in allergy. These hormone-like proteins regulate the expansion of inflammatory cells in asthma, allergy and parasite infections. We study three cytokines (IL-3, IL-5 and GM-CSF) which share a common signalling receptor (beta common receptor) and collectively regulate allergic inflammation and the expansion of granulocytes (neutrophils, basophils and eosinophils), mast cells and macrophages. One major aim is to study how the cytokines activate their receptor systems by binding to the receptors on the outside of cells and transmit intracellular signals which promote growth, differentiation, survival and activation of leukocytes. We use the techniques of protein expression, crystallization and X-ray crystallography to determine the structure of the receptors and site-directed mutagenesis to elucidate function. We are also interested in revealing the molecular mechanisms which promote self-renewal and differentiation of blood cell progenitors. A particular interest is the regulation of differentiation of inflammatory cells in asthma by microRNAs. These tiny RNAs show enormous promise as targets for the treatment of a variety of human diseases and the possibility of modulating their activity as a new anti-inflammatory treatment for asthma is one of our major current interests. We also have discovered receptor isoforms of the IL-3 receptor which give two distinct modes of signalling promoting growth and differentiation. The IL-3 receptor alpha is known to be over-expressed in acute myeloid leukemia where differentiation of myeloid progenitors is blocked and also to be a marker of leukemic stem cells. This receptor is currently a therapeutic target. We are interested in determining the role of the IL-3 receptor system in acute myeloid leukemia.