NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

SEMINAR

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Regulation of apoptotic cell death and other vital processes by the BCL-2 protein family

By **Andreas Strasser**

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Apoptotic cell death is critical for embryonic development, tissue homeostasis after birth, immune defence against infectious pathogens, tumour suppression and other processes of life. Apoptotic cell death is controlled by the BCL-2 family of proteins, containing pro-survival proteins, such as BCL-2 and MCL-1, the effectors of apoptosis (BAX, BAK) and the initiators of apoptosis, such as BIM and PUMA. Based on studies using cancer derived cell lines and protein over-expression it has been proposed that at least some pro-survival proteins, in particular MCL-1, have critical apoptosis unrelated functions in addition to their canonical anti-apoptotic roles. The importance of such apoptosis unrelated roles has not yet been confirmed or even explored in normal physiology. We have now done this by generating so-called gene-swap mice in which for example the coding region for MCL-1 in its endogenous locus was replaced with the coding region for BCL-2, BCL-XL or A1. The examination of these gene-swap mice demonstrates for the first time that in addition to its well-known role in inhibiting apoptotic cell death, MCL-1 also has an apoptosis unrelated function that is essential for embryonic development and life after birth. These findings have important implications for the development of MCL-1 inhibitors for cancer therapy.

About the Speaker

Andreas Strasser was trained during his PhD as an immunologist at the Basel Institute for Immunology in Switzerland. He then conducted postdoctoral studies with Prof Suzanne Cory in cancer and molecular biology at The Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, where he now heads the Blood Cells and Blood Cancer Division. He discovered that defects in programmed cell death can promote the development of cancer or autoimmune disease and can render malignant cells resistant to diverse anti-cancer therapeutics. His discovery of the functions of BH3-only proteins as essential initiators of apoptosis directly underpinned the development of BH3 mimetic drugs for cancer therapy, with the BCL-2 inhibitor Venetoclax already used in the clinic for treatment of several tens of thousands of patients with chronic lymphocytic leukaemia (CLL) or acute myeloid leukaemia (AML).