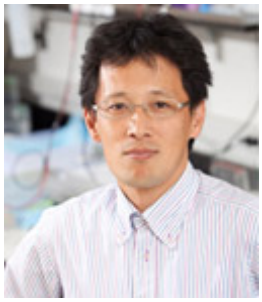
NCGG SEMINAR

Lymphocyte proliferation in protective immunity and oncogenesis



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The 2nd floor Conference Hall Small, 1st Research Building of NCGG

Clonal expansion of lymphocytes is an essential process for both the development of lymphocytes with diverse antigen receptor repertoires and adaptive immunity. Lymphocyte precursors undergo rapid clonal expansion during their development to establish diverse antigen (Ag)-receptor repertoires. During immune responses, Ag-specific T and B cells that are present under steady state conditions at very low frequencies increase their numbers by rapid clonal expansion. Such robust increase in cell numbers is essential to quantitatively amplify their immune responses and as well as to generate high-affinity, mutated antibodies in the germinal centers (GCs). However, clonal expansion is a metabolically demanding process that requires extensive biogenesis. Proliferating lymphocyte precursors and GC B cells are also exposed to substantial genomic insults associated with activities of RAG and AID proteins, leading to the elevated risk of oncogenic transformation. Lymphocytes may thus employ unique programs to facilitate their clonal expansion while minimizing collateral genome damage. However, our knowledge about these regulatory pathways remains limited. To address this question, we have studied gene expression programs initiated by the transcription factor c-MYC, which is essential for proliferation of normal lymphocytes and implicated in oncogenesis. Through these studies, we have identified MYC downstream gene expression programs that facilitate requisite clonal expansion of lymphocytes for protective immunity and protect proliferating lymphocytes from oncogenesis. These findings not only reveal the genetic pathways critical for host protection from infection but also provide the first example of a MYC-inducible tumor suppressor program.

References:

Chou C, Pinto AK, Curtis JD, Persaud SP, Cella M, Lin CC, Edelson BT, Allen PM, Colonna M, Pearce EL, Diamond MS, Egawa T. c-Myc-induced transcription factor AP4 is required for host protection mediated by CD8+ T cells. *Nat Immunol.* 2014 Sep;15(9):884-93.

Chou C, Verbaro DJ, Tonc E, Holmgren M, Cella M, Colonna M, Bhattacharya D, Egawa T. The Transcription Factor AP4 Mediates Resolution of Chronic Viral Infection through Amplification of Germinal Center B Cell Responses. *Immunity.* 2016 Sep 20;45(3):570-582.

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