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A novel aging-associate B-cell subset controls antitumor CD8+ T-cell response

Catalina Lee-Chang
National Institute on Aging, NIH, USA

CD8+CD28- T cells are considered an immune risk of mortality and morbidity in elderly. The mechanism of their enrichment and their function in elderly is poorly understood. In the present study we report a novel and evolutionary-conserved B-cell subset expressing 4-1BBL, which accumulates with aging of mammals, such as humans, rhesus macaques and mice. These cells (termed 4BL cells) induce antitumor effector CD8+ T cells by presenting endogenous antigens and utilizing 4-1BBL/4-1BB axis. 4BL cells are also responsible for the expansion of auto-reactive CD8+ T cells in patients treated with high dose chemotherapy and autologous progenitor cell transplantation. Thus, accumulation of anti-tumor 4BL cells explains the paradox of retarded tumor growth in the elderly, and most likely autoimmune disease outcome in the aged population. However, 4BL cell accumulation and their effects on CD8+ T-cell compartment can be eliminated by inducing B-cell lymphopoiesis in old mice (after B-cell depletion), suggesting that the aging-associated skewed cellular immune responses are reversible. We propose that 4BL cells and their 4-1BBL signaling pathway are useful targets for improved effectiveness of natural antitumor defenses and therapeutic immune manipulations in the elderly. How 4BL are generated, and their impact in the B-cell effector functions homeostasis in elderly will be further discussed.

Biography

Catalina Lee-Chang has completed her PhD in Immunology from University of Lille Nord de France in 2010. Her work focused on the role of B cells in multiple sclerosis pathogenesis and neuroinflammatory mechanism. In 2011 she joined Arya Biragyn's lab (NIH) as Postdoc to continue her training in B-cell biology, as well as cancer and aging immunology.

catalina.leechang@nih.gov