

CONCOMMITTANT EXPRESSION OF CD40 AND CD154 BY THE AT-HOOK PROTIEN AKNA MAY PROVIDE A SURVIVAL ADVANTAGE TO CHRONIC LYMPHOCYTIC LEUKEMIA. Jennifer Sims-Mourtada, Roberto Rangel, Lilliana Guzman-Rojas, Christina Lopez, Kelly Cain and Hector Martinez-Valdez. Department of Immunology, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030.

Chronic lymphocytic leukemia (CLL) is the most frequent adult leukemia in America. Earlier studies demonstrated that CLLs strongly co-express CD40 and CD154, essential signaling molecules for B cell growth and survival. CLL's are capable of undergoing homotypic signaling through CD40 and CD154 providing autocrine growth and survival signals that lead to tumor progression and persistence. Furthermore, CLL expressed CD154 is capable of providing T cell- like costimulation in a paracrine fashion leading to selection of B cells that would normally undergo apoptosis, possibly contributing to autoimmune diseases associated with CLL. Co-expression of CD40 and CD154 predicted a common regulatory mechanism for the receptor and its ligand. The discovery of the human transcription factor AKNA, which is capable of simultaneously regulating CD40 and CD154 and the finding of its strong expression by CLLs, prompted us to hypothesize that dysregulation of AKNA expression is a risk factor that can lead to enhanced CLL growth and survival. The finding that AKNA gene is localized to a region of high genomic instability, chromosome 9q32, further supports our hypothesis of aberrant expression of AKNA during malignancy.