

## CORRELATION BETWEEN THE LEVEL OF HISTONE ACETYLATION AND $V_H$ GENE REARRANGEMENT FREQUENCY

Celia R. Espinoza and Ann J. Feeney, Department of Immunology, The Scripps Research Institute, La Jolla CA

The process of V(D)J recombination is an essential element of lymphocyte differentiation and is under very tight lineage-specific and stage-specific control. One level of control of accessibility to the recombinase enzymes is by posttranslational modification of the histones. We have examined the accessibility of individual genes in the murine IgH locus in freshly isolated pro-B cells from MT mice. We have previously shown that the three  $V_H$  genes in the murine  $V_H$ S107 family arrange at very different frequencies in pro-B cells *in vivo*. Using chromatin immunoprecipitation, we have analyzed the level of acetylation of histones associated with those three  $V_H$  genes in pro-B cells. We observed that the extent of enrichment of the three V genes in the immunoprecipitated fraction is directly proportional to their relative rearrangement frequency *in vivo*. We extended this analysis to the  $V_H$ 7183 family, where the  $D_H$ -proximal 81X gene rearranges at an extraordinarily high frequency in fetal development, and even rearranges frequently in the adult bone marrow. We analyzed the acetylation status of the histones associated with 81X and compared that to the rest of the  $V_H$ 7183 genes using a family specific primer which excluded 81X. The level of acetylation was higher for histones associated with 81X than for the other  $V_H$ 7183 genes, and this ratio was increased in DNA derived from newborn liver pro-B cells. Thus, we conclude that the acetylation status of histones associated with individual V genes varies, and this variation may contribute to the non-random V gene usage observed in the initial repertoire.