**Changes of chromosomal architecture in immune cells**

Naive CD4 T cells differentiate into several effector lineages, which generate a stronger and more rapid response to previously encountered immunological challenges. Although effector function is a key feature of adaptive immunity, the molecular basis of this process is poorly understood. Here, we investigated the spatiotemporal regulation of cytokine gene expression in resting and restimulated effector T helper 1 (Th1) cells. We found that the Lymphotoxin (LT)/TNF alleles, which encode TNF-α, were closely juxtaposed shortly after T-cell receptor (TCR) engagement, when transcription factors are limiting. Allelic pairing required a nuclear myosin, myosin VI, which is rapidly recruited to the LT/TNF locus upon restimulation. Furthermore, transcription was paused at the TNF locus and other related genes in resting Th1 cells and released in a myosin VI-dependent manner following activation. We propose that homologous pairing and myosin VI-mediated transcriptional pause release account for the rapid and efficient expression of genes induced by an external stimulus.