

Very simply put, cancer is a disease of aberrant gene regulation. One of the most important controls points in the flow of genetic information from the genome is transcription. A central goal of work in my lab has been to define and elucidate mechanisms of transcriptional control in lymphoid cells. Our most recent focus has been on two transcriptional regulators that play very important roles in the evolution and progression of cancer, the histone acetyl-transferase p300 and the early onset breast cancer gene BRCA1. I will present data in which we have used genome location analysis ("ChIP/Chip", the combination of chromatin immuno-precipitation and micro-array technology) as the first step in defining mechanisms of transcriptional control. In the case of p300 I will present data indicating a vital role for this co-regulator in multiple steps during the transcriptional regulation of immediate early gene expression by facilitating both pre-initiation complex recruitment and transcriptional elongation. Of note will be the role of transcriptional elongation factors that have been implicated in leukemogenic chromosomal translocations. I will also present new information on the use of ChIP/Chip to identify direct transcriptional targets of BRCA1 and define how these interactions may influence gene expression in response to both DNA damage and cell cycle progression.