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YY1 controls long range DNA interactions of Ig heavy chain locus during class-switch recombination

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B lymphocyte development involves a temporal order of long-range DNA recombination events that results in the assembly of variable (V), diversity (D) and joining (J) gene segments to produce functional Ig genes. In activated splenic B cells and germinal center cells, somatic hypermutation and class switch recombination (CSR) regulate IgH expression. The rearrangement of distal V genes requires locus contraction and DNA looping and studies showed that YY1-/- pro-B cells have greatly impaired distal VH gene rearrangement and IgH locus compaction. Studies have shown that YY1 is essential for B cell development and we have shown that numerous long range DNA loops are also required for CSR and loss of YY1 significantly reduces CSR. CSR involves DNA looping between the intronic enhancer (Eμ) and the 3'RR enhancer. This Eμ - 3'RR synapse is dependent on YY1 as measured by 3C and 3D-FISH assays, as well as by ChIP-seq. We performed ChIP-seq with splenic B cells to investigate whether YY1 colocalizes with condensins, cohesins and PcG proteins to understand the mechanism of YY1 mediated locus contraction. The raw sequences were analyzed using bowtie2. The Homer software package was used to analyze the aligned reads for regions of over representation of read depth (peaks) utilizing the find Peaks factor program and statistical significance was determined by using a FDR of 1%, 4-fold reads in peak over background, and requiring a cumulative poisson p-value of 0.0001. Our data indicated that SMC4, Rad21 and EZH2 bind at the 3'RR hs4 site along with YY1.

Biography

Arindam Basu has completed his PhD from Indian Institute of Science (IISc), Bangalore in India and continued his Post-doctoral research on gene expression and regulation in the laboratory of Dr. Michael L. Atchison at the University of Pennsylvania. He is currently an Assistant Professor at Penn State University, Brandywine campus where he teaches undergraduate courses. His primary research interests have been in the area of epigenetic regulation by Polycomb group of proteins and long-range DNA interactions. He has published several papers demonstrating the role of Polycomb proteins in chromatin organization.

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