Chromatin Immunoprecipitation Sequencing (ChIP-seq)

Chromatin Immunoprecipitation, first described by Varshavsky and colleagues (1), is a method to study DNA-protein interactions in four basic steps (Figure 1). First, covalent crosslinks are induced between DNA and neighboring proteins by treating cells with formaldehyde. Second, crosslinked DNA is sheared into fragments. Third, antibodies to the protein of interest are used to selectively immunoprecipitate and purify the protein-DNA fragments that are covalently crosslinked. Finally, the crosslinks are reversed in the immunoprecipitated sample, allowing the released DNA fragments to be analyzed to determine the sequences bound by the protein of interest. Through this process, random crosslinking can also occur which links DNA with proteins that are not specifically bound and results in non-specific pull down of DNA fragments not associated with the protein of interest. Therefore, parallel samples wherein no antibody selection has taken place are typically included. Historically, these two DNA populations are compared to identify specific DNA-protein binding events and analyzed by PCR, microarray (ChIP-chip; 2), and now, as templates for next generation sequencing (ChIP-seq; See Gennovations, Volume 1, Issue 1).

The short DNA fragments retrieved from ChIP are ideally suited for sequencing on the next generation platforms. Specifically, the short ~35 nucleotide read lengths obtained using the Illumina platform are optimal for sequencing ChIP-derived fragments. Furthermore, there is limited hybridization bias that is inherent in microarray studies, and the data provides a global view of the sequences bound by the protein of interest. Next generation sequencing allows for lower cost than microarrays, minimal hands-on processing and the requirement for fewer replicates.
References and for more information: