

NimbleGen ChIP-chip Scientific Publications

Chromatin immunoprecipitation on DNA chips (ChIP-chip) has caught the attention of an increasing number of researchers, allowing them to study promoter/enhancer discovery, transcription factor binding, histone modification/replacement, and DNase-I hypersensitivity on a genome-wide scale. NimbleGen has established itself as the leader in the ChIP-chip field, as evidenced by the number of high-profile, peer-reviewed publications describing studies utilizing our platform. A subset of NimbleGen ChIP-chip scientific publications is included below. For a complete list, see www.NimbleGen.com.

References	Notes
Genomic Element Identification	
Kim, T.H., <i>et al.</i> (2007) Analysis of the vertebrate protein CTCF-binding sites in the human genome. <i>Cell</i> 128, 1231-1245.	NimbleGen whole-genome tiling arrays and custom arrays were used to describe 13,804 CTCF-binding sites in potential insulators of the human genome in primary human fibroblasts. Their results provide a resource for investigating insulator function and possible other general and evolutionarily conserved activities of CTCF sites.
Heintzman, N.D., <i>et al.</i> (2007) Distinct and predictive chromatin signatures of transcriptional promoters and enhancers in the human genome. <i>Nat Genet</i> 39(3), 311-318.	Using NimbleGen ENCODE arrays, the chromatin modification states of active promoters, which are marked by trimethylation of Lys4 of histone H3 (H3K4), were determined. Enhancers are marked by monomethylation, but not trimethylation, of H3K4.
Jin, V.X., <i>et al.</i> (2006) A computational genomics approach to identify cis-regulatory modules from chromatin immunoprecipitation microarray data--A case study using E2F1. <i>Genome Res</i> 16(12), 1585-1595.	Using NimbleGen ENCODE ChIP-chip arrays against E2F1, these researchers developed a computational genomics approach (termed ChIPModules), which uses experimentally determined binding sites, a comparative genomics approach, and statistical learning methods to identify transcriptional regulatory modules.
Kim, T.H., <i>et al.</i> (2005) A high-resolution map of active promoters in the human genome. <i>Nature</i> 436(7052), 876-880.	The first human whole-genome ChIP-chip study using NimbleGen's whole-genome tiling array set and a custom array focusing on putative peaks. The data from four different antibodies (TAF1, Pol II, ACh3 and H3K4me3) highly correlate with each other, with over 96% overlap on known promoters.
Transcription Factor Binding	
Krig, S.R., <i>et al.</i> (2007) Identification of genes directly regulated by the oncogene ZNF217 using ChIP-chip assays. <i>J Biol Chem</i> Published online: 26 January 2007.	A whole-genome ChIP-chip scan demonstrated that ZNF217 acts as a transcriptional repressor for many genes in Ntera2 cells. This oncogene may function as a repressor of organ differentiation.
Navarre, W.W., <i>et al.</i> (2006) Selective silencing of foreign DNA with low GC content by the H-NS protein in Salmonella. <i>Science</i> 313(5784), 236-238.	Study demonstrating that the histone-like nucleoid structuring protein (H-NS) selectively silences horizontally acquired genes in Salmonella by targeting sequences with low GC content in the genome. This H-NS targeting is likely a bacterial defense against foreign DNA.
Thibaud-Nissen, F., <i>et al.</i> (2006) Development of Arabidopsis whole genome microarrays and their application to the discovery of binding sites for the TGA2 transcription factor in salicylic acid-treated plants. <i>Plant J</i> 47(1), 152-162.	The first ChIP-chip study in plants. Both promoter arrays and whole-genome tiling arrays were used for high-throughput identification of transcription factor binding sites.
Scacheri, P.C., <i>et al.</i> (2006) Genome-wide analysis of menin binding provides insights into MEN1 tumorigenesis. <i>PLoS Genet</i> 2(4), e51.	A custom tiling array established that menin binding is highly specific to 5' regions of genes. A second array focusing on such regions allowed the nearly genome-wide study of menin binding.
Bieda, M., <i>et al.</i> (2006) Unbiased location analysis of E2F1-binding sites suggests a widespread role for E2F1 in the human genome. <i>Genome Res</i> 16(5), 595-605.	Both E2F1 and MYC have numerous binding sites throughout the genome. Most E2F1 sites occur at proximal promoter (<1Kb), while nearly half of MYC sites are located more than 10Kb away from transcription start sites (TSS). Thus, NimbleGen promoter arrays are suitable for studying E2F1 binding, but a genome-tiling array is required for an unbiased study of MYC binding.
O'Geen, H., <i>et al.</i> (2006) Comparison of sample preparation methods for ChIP-chip assays. <i>BioTechniques</i> 41, 577-580.	A comparison of preparation methods, including ligation-mediated PCR (LM-PCR) and whole-genome amplification (WGA), uses NimbleGen ENCODE ChIP-chip arrays to identify Oct4 factor binding. These researchers find that the signal-to-noise ratio using the WGA method is superior to LM-PCR.
Chromatin Structure	
Bracken, A.P., <i>et al.</i> (2006) Genome-wide mapping of Polycomb target genes unravels their roles in cell fate transitions. <i>Genes Dev</i> 20(9), 1123-1136.	Potential target genes identified from expression arrays were validated by ChIP-chip using custom tiling of the promoter regions.
Squazzo, S.L., <i>et al.</i> (2006) Suz12 binds to silenced regions of the genome in a cell-type-specific manner. <i>Genome Res</i> 16(7), 890-900.	NimbleGen provided five different arrays for this study. ChIP-chip was performed in different organisms focusing on different regions as directed by their findings.
Kirmizis, A., <i>et al.</i> (2004) Silencing of human polycomb target genes is associated with methylation of histone H3 Lys 27. <i>Genes Dev</i> 18(13), 1592-1605.	An example of integrated genomics; ChIP-chip promoter arrays combined with expression data from RNAi treated samples aided in identifying direct polycomb target genes.
DNase-I Hypersensitivity	
Follows, G.A., <i>et al.</i> (2006) Identifying gene regulatory elements by genomic microarray mapping of DNaseI hypersensitive sites. <i>Genome Res</i> 16, 1310-1319.	Custom arrays spanning the α -globin locus were used in the development of a novel genomic array-based approach to DNaseI hypersensitive site mapping (ADHM).
Crawford, G.E., <i>et al.</i> (2006) DNase-chip: a high-resolution method to identify DNase-I hypersensitive sites using tiled microarrays. <i>Nat Methods</i> 3(7), 503-509.	Biotin was used to tag the DNA ends from DNase-I digestion. DNase-chip results correlated well with MPSS (massively parallel signature sequencing) data from the same group, but had a higher coverage.
Sabo, P.J., <i>et al.</i> (2006) Genome-scale mapping of DNase I sensitivity in vivo using tiling DNA microarrays. <i>Nat Methods</i> 3(7), 511-518.	Researchers used the DNase-array method to measure DNase-I hypersensitivity sites. NimbleGen ENCODE arrays were used in both studies to generate a representative view of the human genome.

Nucleosome Mapping	
Ozsolak, F., <i>et al.</i> (2007) High-throughput mapping of the chromatin structure of human promoters. <i>Nat Biotechnol</i> 25(2), 244-248.	NimbleGen high-resolution (10bp spacing) arrays looking at 3,692 promoters, demonstrated that expressed genes exhibit nucleosome-free regions at their transcription start sites. The melanocyte transcription factor MITF predominantly binds nucleosome-free regions, supporting the model that nucleosomes limit accessibility.
Dosage Compensation	
Ercan, S., <i>et al.</i> (2007) X chromosome repression by localization of the <i>C. elegans</i> dosage compensation machinery to sites of transcription initiation. <i>Nat Genet</i> 39(3), 403-408.	The binding sites of two components of the <i>C. elegans</i> dosage compensation complex (DCC), were identified using ChIP-chip whole-genome arrays. This study aids in understanding how proteins involved in higher-order chromosome dynamics can regulate transcription at individual loci.
Alekseyenko, A.A., <i>et al.</i> (2006) High-resolution ChIP-chip analysis reveals that the <i>Drosophila</i> MSL complex selectively identifies active genes on the male X chromosome. <i>Genes Dev</i> 20(7), 848-857.	The MSL-3 protein was tagged by TAP (containing two IgG binding domain of Protein A) and immunoprecipitated by IgG beads.
Giffillan, G.D., <i>et al.</i> (2006) Chromosome-wide gene-specific targeting of the <i>Drosophila</i> dosage compensation complex. <i>Genes Dev</i> 20(7), 858-870.	Antibodies against native MSL-1 were used to perform ChIP. This publication, using a different ChIP approach, reached the same conclusion as the publication immediately above.
Histone Variant Replacement	
Mito, Y., <i>et al.</i> (2007) Histone replacement marks the boundaries of cis-regulatory domains. <i>Science</i> 315(5817), 1408-1411.	NimbleGen arrays were used to examine nucleosome occupancy and histone replacement at <i>Drosophila</i> homeotic gene clusters. These results suggest the existence of a continuous process that disrupts nucleosomes and maintains accessibility of cis-regulatory elements.
Mito, Y., <i>et al.</i> (2005) Genome-scale profiling of histone H3.3 replacement patterns. <i>Nat Genet</i> 37(10), 1090-1097.	This study presents a novel strategy to map epigenetic patterns: H3.3 variant was tagged with biotin, and its replacement pattern in the genome was studied using a NimbleGen high-density tiling array.

NimbleGen and the ENCODE Consortium

ENCODE (the Encyclopedia Of DNA Elements), a public research consortium launched by the National Human Genome Research Institute (NHGRI), aims to functionally annotate elements in the human genome sequence (www.genome.gov/10005107; *Science* 306(5696), 636-640). This is the largest public collaboration in which ChIP-chip is being utilized as a major technology to generate data. The ENCODE consortium requires that all ChIP-chip data be of the highest quality. Because of NimbleGen's superior sensitivity, specificity, and reproducible ChIP-chip platform, the majority of researchers in the consortium use our arrays to perform ChIP-chip and DNase-I hypersensitivity assays.



This screen shot from the UCSC genome browser (genome.ucsc.edu/ENCODE/encode.hg17.html), the official repository of sequence-related data for the ENCODE consortium, displays chromatin immunoprecipitation and chromosome, chromatin, and DNA structure data generated by ENCODE consortium members.

Data generated on the NimbleGen platform is circled in red.