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Data in Brief

Genome wide mapping of Foxo1 binding-sites in murine T lymphocytes

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ABSTRACT

The Forkhead box O (Foxo) family of transcription factors has a critical role in controlling the development, differentiation, and function of T cells. However, the direct target genes of Foxo transcription factors in T cells have not been well characterized. In this study, we focused on mapping the genome wide Foxo1-binding sites in naïve $CD4^+$ T cells, $CD8^+$ T cells, and $Foxp3^+$ regulatory T (Treg) cells. By using chromatin immunoprecipitation coupled with deep sequencing (ChIP-Seq), we identified Foxo1 binding sites that were shared among or specific to the three T cell populations. Here we describe the experiments, quality controls, as well as the deep sequencing data. Part of the data analysis has been published by Ouyang W et al. in Nature 2012 [1] and Kim MV et al. in Immunity 2013 [2], and the associated data set were uploaded to NCBI Gene Expression Omnibus.

Specifications	
Organism/cell line/tissue	*Murine T cells*
Sex	*Male or female*
Sequencer or array type	*Illumina Genome Analyzer IIx*
Data format	*Analyzed*
Experimental factors	*Foxo1 antibody and Streptavidin were used for ChIP*
Experimental features	*ChIP DNAs were prepared from T cells isolated from C56BL/6 mice using Foxo1 antibody and T cells isolated from Foxo1tag/tagbirA mice using Streptavidin-coated beads. ChIP-seq libraries were prepared following a standard protocol.*
Consent	*N/A*
Sample source location	*N/A*

Direct link to deposited data

http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE60470
http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE40657
http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE46944

Experimental design, materials and methods

Mice

Normal C57BL/6 mice and mice containing *Foxo1 knock-in* (Foxo1tag), *Foxp3-IRES-RFP* and *birA* alleles or *Foxp3-IRES-RFP* and *birA* alleles were previously described [1]. Treg cells in mice carrying the *Foxp3-IRES-RFP* allele were marked by red fluorescence protein (RFP). Foxo1 in mice carrying the Foxo1tag and birA alleles was labeled by biotin. All mice were maintained under specific pathogen-free conditions, and animal experimentation was conducted in accordance with institutional guidelines.

Chromatin immunoprecipitation (ChIP)

$CD44^-$ $CD62L^{hi}$ naïve $CD4^+$ T, $CD8^+$ T, and $Foxp3^+$ Treg cells were isolated by FACS-sorting, and then fixed for 10 min at 25 °C with 10% formaldehyde. After incubation, glycine was added to a final concentration of 0.125 M to 'quench' the formaldehyde. Cells were pelleted, washed twice with ice-cold PBS and lysed. The lysates were pelleted, re-suspended and sonicated to reduce DNA length to 300–500 base pairs (bp). The chromatin prepared from T cells of C57BL/6 mice was incubated with protein-A-anti-Foxo1 (ab39670, Abcam) or an isotype control antibody overnight. The chromatin prepared from T cells of Foxo1tag/tag birA Foxp3-IRES-RFP or control birA mice was incubated with streptavidin overnight. The immune complexes were washed, and eluted in 500 μl of elution buffer containing 50 mM Tris, 10 mM EDTA and 1.0% SDS. Precipitated ChIP DNA and input DNA were incubated at 65 °C to reverse the crosslinking. After digestion with RNase and

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proteinase K, the ChIP and input DNA were purified with phenol/chloroform extraction and ethanol precipitation. The purified DNA was repaired, ligated with an adaptor, and amplified by PCR for 15–20 cycles. The amplified DNA was purified by gel extraction and used for sequencing. SR-36 sequencing was done at the Genome Center of Cold Spring Harbor Laboratory.

Data analysis

Initial quality control of the sequencing was performed using FastQC (http://www.bioinformatics.babraham.ac.uk/projects/fastqc/). After verifying acceptable base calling quality, nucleotide distribution, and adapter contamination, reads were aligned to the mouse mm9 (NCBI, Build 37, July 2007) reference genome obtained through the UCSC Table Browser (http://genome.ucsc.edu/) using version 0.12.7 of the Bowtie short read alignment software [3] (http://bowtie-bio.sourceforge.net/index.shtml). The parameters "—k 1–m 1" were used to select for only uniquely mapping reads. Peak calling was then performed on the aligned reads. For the $CD4^+$ and T_{reg} cell-types, MACS [4] (version 1.4.1, http://liulab.dfci.harvard.edu/MACS/) was used to identify putative binding sites. MACS makes use of the inherent tendency of clusters of sense and antisense reads flanking protein-DNA interaction sites to model fragment length. It then considers this estimate when defining windows used to scan the genome for enrichment according to a Poisson distribution. For the analysis of the $CD8^+$ data, we developed a novel peak-calling algorithm BCP [5] (http://rulai.cshl.ed/BCP/), which employs a Bayesian Hidden Markov model, to perform segmentation of the genome and identify enrichment. This method expands peak-calling capabilities to more diffuse, less punctate enrichment, as seen in many histone modification ChIP-seq and DNase I hypersensitivity sequencing assays. Because BCP does not have an integrated method for dealing with potential PCR duplicates, we preprocessed the read alignments to include only one instance of each unique chromosome start and end position. In both cases, we employed the empirical FDR (eFDR) metric as described by Yong, Z., et al. [4] to minimize false positives. This entailed using the input alignments as the treatment data and the ChIP alignments as the control to infer the background peak-calling rate. The p-value of peak calling used by MACS or BCP was then adjusted to ensure that the fraction of background peaks divided by called peaks did not exceed the eFDR threshold. This was set to 0.01 for MACS but 0.05 for BCP since, in our experience, it was less sensitive to low density peak false calls. The BEDtools suite of utilities [6] was used for post-processing tasks such as finding overlapping antibody and biotin immunoprecipitated peaks. Visualization was performed using custom R scripts.

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