Data in Brief

p53 transcriptional programs in B cells upon exposure to genotoxic stress in vivo: Computational analysis of next-generation sequencing data

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Abstract

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The transcriptional programs activated by p53 in B cells in vivo following exposure to ionizing radiation were studied through the integrated analysis of various types of next-generation sequencing data: genome-wide profiling of p53 binding sites, mapping of histone marks and open chromatin regions and quantification of gene expression. Moreover, the binding of p53 was associated to a series of specific motifs on the DNA, which were directly inferred from the data. Here, we describe in detail the computational analysis of the datasets associated with our study (Tonelli et al., Oncotarget 6 (2015), 24611-26), deposited in the GEO archive (accession code GSE71180), and we provide the R scripts needed to generated the figures of the paper.

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1. Direct link to deposited data

http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE71180.

2. Experimental design, materials and methods

The GEO submission SuperSeries GSE71180, associated with the Tonelli et al. study [1], contains a total of 32 NGS samples, divided in three series: GSE71775, containing 6 ChIP-Seq samples (5 ChIP against p53 and one Input); GSE71776, containing 24 RNA-Seq samples (4 conditions with 2 replicates each for the p53 KO cells, 4 conditions with 4 replicates each for the C57/B6 cells); GSE71777, containing a DNase-Seq sample and the corresponding input. The datasets are summarized in Table 1.

These samples allowed studying the genomic occupancy and the transcriptional changes induced by p53 activation in B and non-B cells in vivo, following DNA damage produced by ionizing radiation. Cells from p53 null mice were analyzed to define the p53-dependent response.

3. Data analysis

We complement the methods of the original publication and the instructions deposited in the GEO archive with the source code used to produce the Figures from the Next-Generation Sequencing (NGS) data files. Under the accession number GSE71180, we provided the raw data files (sequencing reads, in fastq format), plus a series of processed data files: for the ChIP-Seq and DNase-Seq samples (excluding the inputs), we supplied the locations of the bound genomic regions in BED format, as obtained with the MACS [2] peak caller (v. 2.0.9), while for the RNA-Seq samples, we provided the quantification of the expression of each gene, i.e. the number of reads assigned to every gene.
Table 1
Summary of the 32 samples available in the GSE71180 SuperSeries.

| Sample ID          | Sample name            | Replicate | Data type       |
|--------------------|------------------------|-----------|-----------------|
| GSM1828855         | p53.wt.Bcells.mock     | 1/1       | ChIP-Seq        |
| GSM1828856         | p53.wt.Bcells.IR       | 1/1       | ChIP-Seq        |
| GSM1828857         | p53.wt.nonBcells.mock  | 1/1       | ChIP-Seq        |
| GSM1828858         | p53.wt.nonBcells.IR    | 1/1       | ChIP-Seq        |
| GSM1828859         | p53.null.spleen.IR     | 1/1       | ChIP-Seq        |
| GSM1828860         | Input                  | 1/1       | ChIP-Seq        |
| GSM1828861         | p53.null.Bcells.mock1  | 1/2       | RNA-Seq         |
| GSM1828862         | p53.null.Bcells.mock2  | 2/2       | RNA-Seq         |
| GSM1828863         | p53.null.nonBcells.mock1 | 1/2   | RNA-Seq         |
| GSM1828864         | p53.null.nonBcells.mock2 | 2/2   | RNA-Seq         |
| GSM1828865         | p53.null.Bcells.IR1    | 1/2       | RNA-Seq         |
| GSM1828866         | p53.null.Bcells.IR2    | 2/2       | RNA-Seq         |
| GSM1828867         | p53.null.nonBcells.IR1 | 1/2       | RNA-Seq         |
| GSM1828868         | p53.null.nonBcells.IR2 | 2/2       | RNA-Seq         |
| GSM1828869         | p53.wt.Bcells.mock1    | 1/4       | RNA-Seq         |
| GSM1828870         | p53.wt.Bcells.mock2    | 2/4       | RNA-Seq         |
| GSM1828871         | p53.wt.Bcells.mock3    | 3/4       | RNA-Seq         |
| GSM1828872         | p53.wt.Bcells.mock4    | 4/4       | RNA-Seq         |
| GSM1828873         | p53.wt.nonBcells.mock1 | 1/4       | RNA-Seq         |
| GSM1828874         | p53.wt.nonBcells.mock2 | 2/4       | RNA-Seq         |
| GSM1828875         | p53.wt.nonBcells.mock3 | 3/4       | RNA-Seq         |
| GSM1828876         | p53.wt.nonBcells.mock4 | 4/4       | RNA-Seq         |
| GSM1828877         | p53.wt.Bcells.IR1      | 1/4       | RNA-Seq         |
| GSM1828878         | p53.wt.Bcells.IR2      | 2/4       | RNA-Seq         |
| GSM1828879         | p53.wt.Bcells.IR3      | 3/4       | RNA-Seq         |
| GSM1828880         | p53.wt.Bcells.IR4      | 4/4       | RNA-Seq         |
| GSM1828881         | p53.wt.nonBcells.IR1   | 1/4       | RNA-Seq         |
| GSM1828882         | p53.wt.nonBcells.IR2   | 2/4       | RNA-Seq         |
| GSM1828883         | p53.wt.nonBcells.IR3   | 3/4       | RNA-Seq         |
| GSM1828884         | p53.wt.nonBcells.IR4   | 4/4       | RNA-Seq         |
| GSM1828885         | p53.wt.Bcells.DNase1   | 1/1       | DNase-Seq       |
| GSM1828886         | Input.DNasel           | 1/1       | DNase-Seq       |

This R script loads all the data files needed to produce the figures of the main paper [1], and contains all the libraries and functions invoked in the R scripts contained in the file TonelliEtAl2015_Figures.R. In particular, the environment requires the following libraries: compEpiTools, ggplot2, VennDiagram, lattice, flashClust, TxDb.Mmuseus.UCSC.m9.knownGene, and org.Mm.eh.db (see sessionInfo.log).

• TonelliEtAl2015_Figures.R

This R script the instructions contained in the file analysisEnvironment.R to load the pre-generated data objects associated with the main paper [1], and contains the code used to produce all the figures referring to the computational analyses of NGS data. Occasionally, some figures require computing tag density on genomic intervals, and therefore require alignment (BAM) files: in these cases, a pre-computed table was used.

• prepareDatasets.R

This collection of R scripts allows complementing the processed ChIP-Seq files available on GEO with the extra fields required for the generation of the final figures. The output of these scripts is contained in the ChIPpeaks.rds datafile in the data directory, under the form of a list of genomic ranges, which is automatically loaded in the analysisEnvironment.R script. The scripts contained in prepareDatasets.R use several external tools (MEME [7], TOMTOM [8] FIMO [9]), the mm9 reference genome, available in Bioconductor in the library BSgenome.Mmuseus.UCSC.m9 (v. 1.4.0), and may require a consistent amount of time (6–24 h) to complete, depending on the platform used. In order to execute the scripts, the processed ChIP-Seq files should first be downloaded from GEO and organized according to the instructions contained in the filmmapping.R file. Subsequently, alignment (BAM) files must be generated from the raw fastq files deposited in GEO, following the instructions on the archive.

The extra fields consist in:

1) the genomic annotation of the p53 ChIP-Seq peaks: a peak overlapping with a \([-5 \text{ kb}, +2 \text{ kb}]\) window around a standard promoter is considered “promoter”, those overlapping with an H3K4me1 peak, “enhancers”; otherwise they are classified as “distal”;
2) the enrichment of the peak: computed with the GRenrichment function in the compEpiTools suite;
3) the summit of the peak: computed with the GcoverageSummit function in the compEpiTools suite;
4) the motif annotation of the peak, which is obtained through five main steps: i) the generation of a FASTA file containing the sequences of the top 1000 enriched genomic regions spanned by the peaks of the p53.wt.Bcells.IR sample; ii) the estimation of the unspaced p53 motif from these sequences using MEME [7] (we verify that the estimated motif coincides with the p53 canonical motif contained in the Jaspar Core Vertebrata database [10] using TOMTOM [8]); iii) the creation of the motifs with spacers, obtained by inserting sequences with constant probability over the 4 nucleotides (spacers) between the two half decameric sites; iv) the scoring of these motifs against the mouse genome with FIMO [9]; v) the assignment of the motifs to the ChIP-Seq peaks.

• SessionInfo.log
A log file containing the output of the R sessionInfo() command, specifying all the versions of all the libraries used in the analysis environment.

- data folder

  This folder contains all the R objects needed to produce the figures of the main paper.

- figures folder

  This folder contains all the figures of the main paper, in pdf format, obtained by running the scripts contained in TonelliEtAl2015_Figures.R.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.gdata.2015.11.006.

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