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| **Key Resources Table** | | | | |
| **Reagent type (species) or resource** | **Designation** | **Source or reference** | **Identifiers** | **Additional information** |
| Cell line (*H. sapiens*) | OE19 | ACACC | 96071721 |  |
| Cell line (*H. sapiens*) | CP-A | ATCC | KR-42421 |  |
| Cell line (*H. sapiens*) | OE19-dCas9-KRAB | Rogerson et. al, 2020 |  | OE19 transfected with vector to express dCas9-KRAB under doxycycline control |
| Antibody | Rabbit monoclonal anti-Erk1/2 antibody | Cell signalling technology | 4695S | (1:1000) |
| Antibody | Donkey anti-mouse secondary antibody (800CW) | Licor | 925 - 32212 | (1:10,000) |
| Antibody | Donkey anti-rabbit secondary antibody (700CW) | Licor | 925–32213 | (1:10,000) |
| Antibody | Mouse anti-Cas9 | Diagenode | C15200229 | (1:10,000) |
| Antibody | Rabbit anti-BRD4 | Abcam | ab128874 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-CTCF | Merck-Millipore | 07-729 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-H3K27ac | Abcam | ab4729 | 0.5µg/2-4x105 cells |
| Antibody | Mouse anti-H3K27me3 | Merck-Millipore | 07-449 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-H3K4me1 | Abcam | ab8895 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-H3K4me2 | Diagenode | pAb-035-010 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-H3K4me3 | Abcam | ab8580 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-H3K36me3 | Diagenode | pAb-058-010 | 0.5µg/2-4x105 cells |
| Antibody | Mouse anti-H4K20me1 | Diagenode | mAb-147-010 | 0.5µg/2-4x105 cells |
| Antibody | Mouse anti-PolII | Abcam | ab817 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-PolII-S2 | Abcam | ab5095 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-PolII-S5 | Abcam | ab5131 | 0.5µg/2-4x105 cells |
| Antibody | Rabbit anti-Med1 | Antibodies.com | A98044/10UG | 0.5µg/2-4x105 cells |
| recombinant DNA reagent | pGL3 reporter vector | Promega | E1761 |  |
| recombinant DNA reagent | hSTARR\_ORI vector | Addgene | 99296 |  |
| Recombinant DNA reagent | pINDUCER20-GFP-AFOS | Britton et. al, 2017 |  | ADS5006 |
| recombinant DNA reagent | pCH110 | Amersham |  |  |
| Recombinant DNA reagent | pMD2.G | Addgene | 12259 |  |
| Recombinant DNA reagent | psPAX2 | Addgene | 12260 |  |
| Sequenced-based reagent | Primers | This study |  | See supplementary file. |
| Commercial assay or kit | Lipofectamine RNAiMAX | Thermofisher | 13778150 |  |
| Commercial assay or kit | Cell Line NucleofectorTM Kit V | Lonza | VCA-1003 | Used on Amaxa™ Nucleofector™ II with program T-020 |
| Commercial assay or kit | Dual-Light™ Luciferase & β-Galactosidase Reporter System | Thermofisher | T1003 |  |
| Commercial assay or kit | SuperScript™ VILO™ Master Mix | Thermofisher | 11755250 |  |
| Commercial assay or kit | PureLink™ Genomic DNA Mini kit | Thermofisher | K182001 |  |
| Commercial assay or kit | HiFi assemly | NEB | E5520S |  |
| Commercial assay or kit | QuantiTect SYBR Green RT-PCR Kit | Qiagen | 204243 |  |
| Commercial assay or kit | RNeasy Plus Mini Kit | Qiagen | 74134 |  |
| Commercial assay or kit | RNase-free DNase set | Qiagen | 79254 |  |
| Commercial assay or kit | Ampure XP beads | Beckman Coulter Agencourt | A63881 |  |
| Commercial assay or kit | TruSeq stranded RNA library kit v2 | Illumina | RS-122–2001 |  |
| Commercial assay or kit | Nextera DNA library prep kit | Illumina | FC-121–1031 |  |
| Commercial assay or kit | Nextera Index kit | Illumina | FC-121–1012 |  |
| Commercial assay or kit | NEBNext high fidelity 2x PCR master mix | NEB | M0541 |  |
| Commercial assay or kit | DNA Clean and Concentrator | Zymo | D4013 |  |
| Commercial assay or kit | Polyfect | Qiagen | 301107 |  |
| Commercial assay or kit | PEG-it | System Biosciences | LV810A-1 |  |
| Commercial assay or kit | Polybrene | EMD Millipore | TR-1003 |  |
| Chemical compound, drug | Doxycycline | Sigma-Aldrich | D3447 | Used at final concentration of 100 ng/mL |
| Chemical compound, drug | N3-kethoxal | Gift from Chuan He |  | Used at 5mM |
| Peptide, recombinant protein | RNase | Sigma | R4642 | Used at 100 μg/mL |
| Peptide, recombinant protein | pA-Tn5 | Epicypher | 15-1017 |  |
| Peptide, recombinant protein | EGF | ThermoFisher | 10450–013 | 5 μg/L |
| Peptide, recombinant protein | Bovine pituitary extract | ThermoFisher | 1E+07 | Used at 50 mg/L |
| Software, algorithm | Trimmomatic | [Bolger et al., 2014](https://elifesciences.org/articles/57189#bib4) | V0.34 | <http://www.usadellab.org/cms/?page=trimmomatic> |
| Software, algorithm | ChromHMM | Ernst and Kellis, 2012 |  |  |
| Software, algorithm | Bowtie2 | [Langmead and Salzberg, 2012](https://elifesciences.org/articles/57189#bib30) | v2.3.0 | <http://bowtie-bio.sourceforge.net/bowtie2/index.shtml> |
| Software, algorithm | STAR | [Dobin et al., 2013](https://elifesciences.org/articles/57189#bib17) | V2.5.4 | <https://github.com/alexdobin/STAR> |
| Software, algorithm | Macs2 | [Zhang et al., 2008](https://elifesciences.org/articles/57189#bib58) | v2.1.1 | <https://github.com/taoliu/MACS> |
| Software, algorithm | DEseq2 | [Love et al., 2014](https://elifesciences.org/articles/57189#bib33) | V1.22.2 | <https://bioconductor.org/packages/release/bioc/html/DESeq2.html> |
| Software, algorithm | TOBIAS | [Bentsen et al., 2020](https://elifesciences.org/articles/57189#bib1) | v0.5.1 | <https://github.com/loosolab/TOBIAS> |
| Software, algorithm | featureCounts | [Liao et al., 2014](https://elifesciences.org/articles/57189#bib31) | V1.6.2 | [http://subread.sourceforge.net](http://subread.sourceforge.net/) |
| Software, algorithm | FastQC |  | v0.11.4 | <https://www.bioinformatics.babraham.ac.uk/projects/fastqc/> |
| Software, algorithm | bedtools | [Quinlan and Hall, 2010](https://elifesciences.org/articles/57189#bib40) | v2.26.0 | <https://bedtools.readthedocs.io/en/latest/> |
| Software, algorithm | DeepTools | [Ramírez et al., 2016](https://elifesciences.org/articles/57189#bib41) | V2.5.0 | <https://deeptools.readthedocs.io/en/develop/> |
| Software, algorithm | Metascape | Zhou et al. 2019 |  | https://metascape.org/gp/index.html |
| Software, algorithm | Homer | [Heinz et al., 2010](https://elifesciences.org/articles/57189#bib25) | v4.9 | <http://homer.ucsd.edu/homer/> |
| Software, algorithm | R | R Core Team (2018) | v3.5.1 | <https://www.r-project.org/> |
| Software, algorithm | GraphPad Prism |  | V8.0 | [www.graphpad.com](http://www.graphpad.com/) |
| Software, algorithm | Morpheus | Broad Institute |  | https://software.broadinstitute.org/morpheus/ |
| Other | Crystal violet | Sigma Aldrich | HT90132 | Used at concentration of 0.1% |
| Other | Gibco RPMI 1640 | ThermoFisher | 52400 |  |
| Other | Gibco fetal bovine serum | ThermoFisher | 10270 |  |
| Other | Gibco penicillin/streptomycin | ThermoFisher | 15140122 |  |
| Other | Keratinocyte SFM (1x) | ThermoFisher | 17005042 |  |