lines, and as proof of principle, the inventors turned to the murine system. Mouse erythroleukemia (MEL) cells depend on BCL11A for an adult-stage pattern of globin gene expression (14). The inventors identified an orthologous erythroid composite enhancer at mouse Bcl11a intron-2. Like the human GWAS-marked intron-2 BCL11A enhancer, these sequences possessed a series of erythroid-specific DHSs. In addition, these sequences were decorated by H3K4me1 and H3K27ac, lacked H3K4me3 and H3K27me3, and occupied by both GATA1 and TAL1 in mouse erythroid chromatin (Fig. 8). Composite regulatory elements including a series of adjacent DHSs have been shown to be critical for gene expression at numerous loci, including among others the β-globin locus control region, α-globin multispecies conserved sequences, and IgH regulatory region (53-55). We observed species-specific unique features of the composite enhancer. For example, The inventors identified the conserved mouse sequences to each of the three human DHSs +62, +58 and +55, and found erythroid DNase I hypersensitivity at the +62 and +55 conserved sequences, however the +58 conserved sequences lacked DNase I hypersensitivity.

[0226] PCR and Southern blotting verified excision of the +50.4-60.4 kb intronic segment of Bcl11a in three unique MEL clones and two unique pro-B lymphocyte clones (Fig. 9). Sanger-sequenced breakpoints were characteristic of TALEN-mediated cleavage with subsequent NHEJ repair (Fig. 10). Upon deletion of the intronic segment, we observed dramatic reduction in BCL11A transcript in the MEL cell clones by RT-qPCR, using primer pairs detecting exon junctions upstream, spanning or downstream of the deletion (Fig. 5A).

Definitions

[0227] For convenience, certain terms employed in the entire application (including the specification, examples, and appended claims) are collected here. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

[0228] As used herein, the phrase “agent that binds the genomic DNA of the cell on chromosome 2 location 60,716,189-60,728,612” refers to small molecules, nucleic acids, proteins, peptides or oligonucleotides that can bind to the location within the genomic DNA (*e.g.,* chromosome 2 location 60,716,189-60,728,612) and represses mRNA or protein expression of BCL11A in a cell by at least 20% compared to the mRNA or protein level of BCL11A in a cell not treated with such an agent. In one embodiment, the agent “interferes with BCL11A interactions with BCL11A binding partners,” as that phrase is used herein.

[0229] As used herein, the term “small molecule" refers to a chemical agent including, but not limited to, peptides, peptidomimetics, amino acids, amino acid analogs, polynucleotides, polynucleotide analogs, aptamers, nucleotides, nucleotide analogs, organic or inorganic compounds