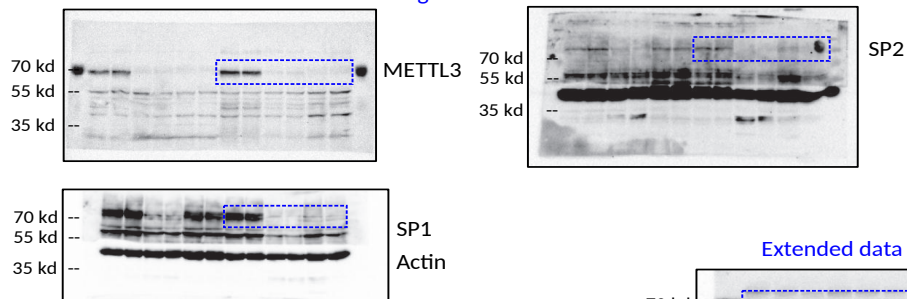
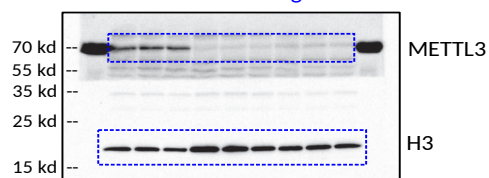


## Full uncropped scans of Western blots

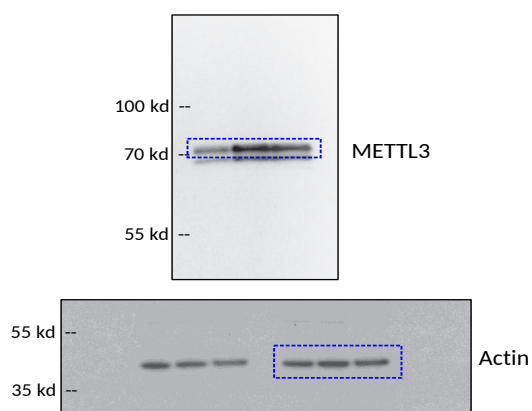
Figure 4a



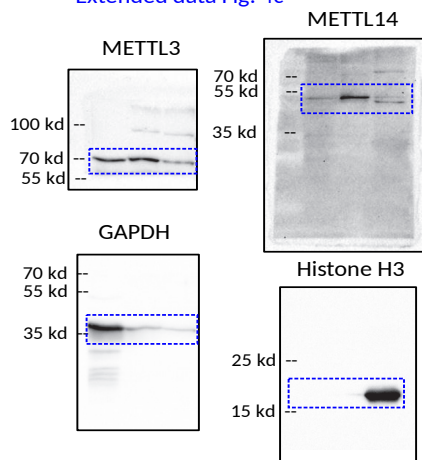
Extended data Fig. 3b



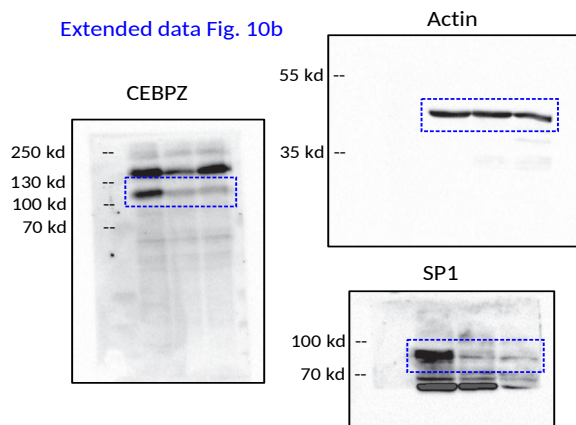
Extended data Fig. 3d



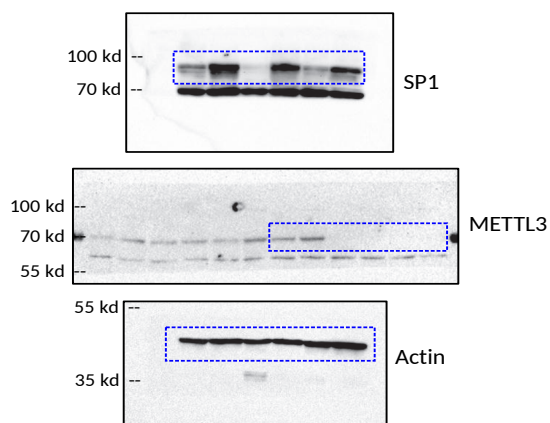
Extended data Fig. 4c



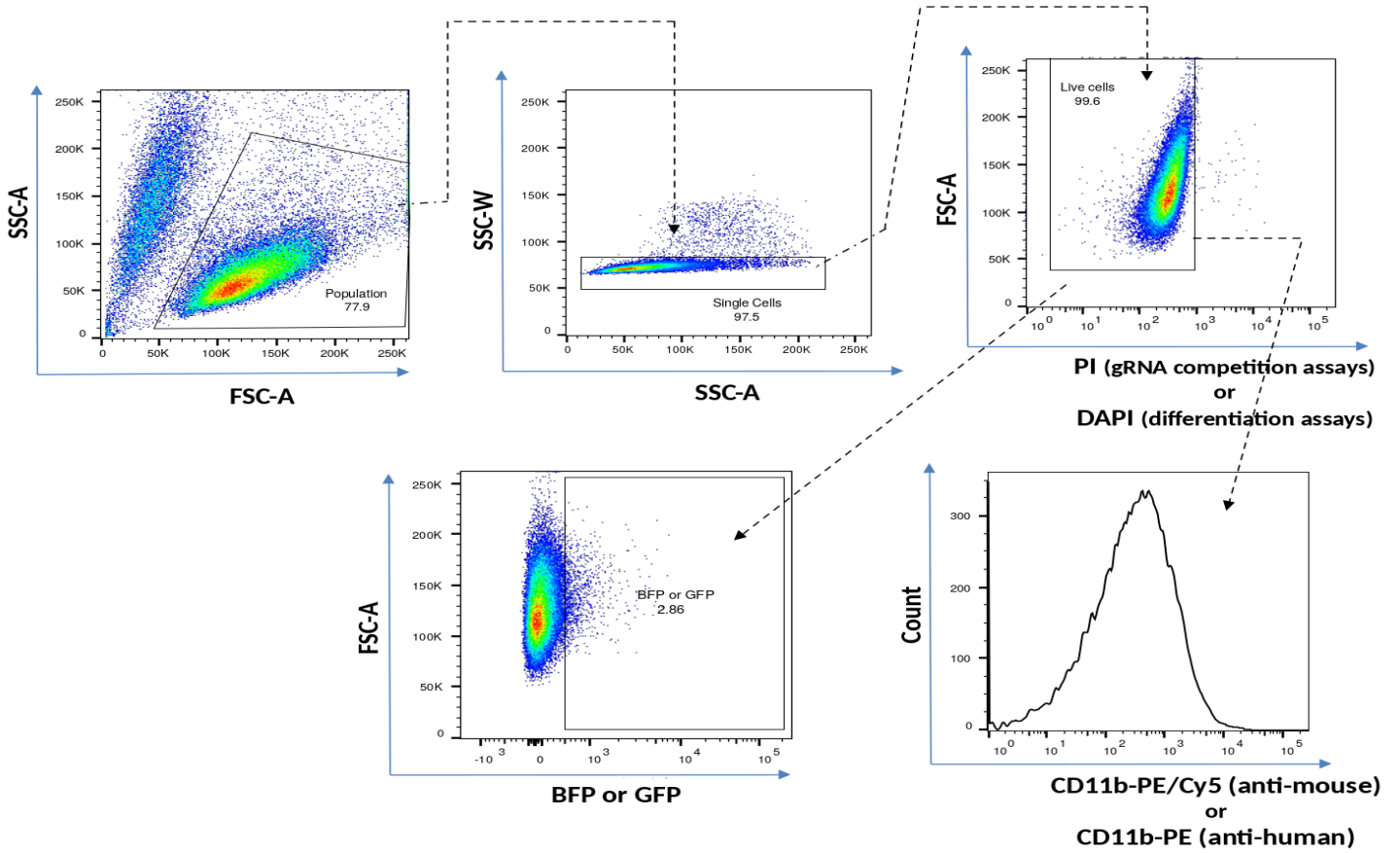
Extended data Fig. 10b



Extended data Fig. 10i



Example of gating strategy employed for flow cytometry experiments



## PRIMERS AND SEQUENCES

Targeted screen validation gRNAs	
Mettl3_52297471_188.15	TTCACATGGAGCTACCGTAT
Mettl3_52296667_106.7	CATCATTAGGACGGGCCGGA
Mettl3_52297471_188.7	CTGTTGTGATATCCGCTACC
Mettl16_74795982_133.3	CCTAGTTCTGTAAACACCGG
Mettl16_74773522_128.5	GATGCCAGATATGCGAAGTC
Mettl16_74787555_141.1	TTACTTGGAGCAACCTTAAA
Mettl14_123374001_62.1	TCGATGAGATTGCAGCACCT
Mettl14_123374745_142.4	ATTCTTCCAGAGGGGGCTCC
Mettl14_123374745_142.11	TCACTGCGAATGAGAAATGC
Emg1_124704981_108.5	ACTGGGAAGTGGTCGGACAC
Emg1_124705515_142.0	GAGGCCACAAAATCGGTCAA
Emg1_124705741_102.7	TTGAAGAATGGACGGGACCC
Tgs1_3602147_144.0	AAGATTGCTGAACACATTGC
Tgs1_3598514_150.1	TTCCAGAGCTGGCTAAATAC
Tgs1_3602147_144.10	ATGTGTTTCAGCAATCTTCTC
Mettl2_105128986_90.1	CTCGGTCACCTAGAAATTAG
Mettl2_105129013_63.0	TCACCTAGAAATTAGTGGTG
Mettl2_105131573_61.1	CTTGAGCAGTTCAATAGCCG
Rpa3_e1.1	ACGGGCCGGTCGATATACTG
Rpa3_e1.2	GACCGGCCCGTGTGCTTCGT
Rpa3_e1.3	GCTGGCGTTGACGCGCGCTT
Rosa26	GAAGATGGGCGGGAGTCTTC

<b>gRNA competition assay</b>	
<b>Mouse gRNAs</b>	
Mettl3_Exonic_A	ACTCGGTCTCGCGACCCTG
Mettl3_Exonic_B	CCGCGATGGTTTCACAGCG
Mettl3_Domain_A	TTCACATGGAGCTACCGTAT
Mettl3_Domain_B	CATCATTAGGACGGGCCGGA
Mettl16_Exonic_A	GAAGATTTGATTGGTCACC
Mettl16_Exonic_B	ACAAACTACTCTCCGAAG
Mettl16_Domain_A	CCTAGTTCTGTAAACACCGG
Mettl16_Domain_B	GATGCCAGATATGCGAAGTC
Sp1	GGGGCTACCCCTACCTCAA
<b>Human gRNAs</b>	
METTL3_Exonic_A	GCAGGGTTCGATCAGCATCAC
METTL3_Exonic_B	GAAATTTTCGCTCTCGAGGTC
METTL3_Domain_A	GCTCAACATACCCGTACTAC
METTL3_Domain_B	CTGTTGTGATATCCGCTACC
METTL16_Exonic_A	GTCAAGGTCGGACAATGAGA
METTL16_Exonic_B	GGGAGGAGCTTCGCATACAA
METTL16_Domain_A	CTCCGAAGAGGAATTGACAT
METTL16_Domain_B	TCAGAGCTCTGACTGCTTCG
METTL1_Exonic_A	GGCTTTGTCCGCTTGAAATG
METTL1_Exonic_B	GGCCTGAGTGTTACCTAAC
METTL14_Exonic_A	GAGGGAGCTCATCAGGCTAA
METTL14_Exonic_B	GAGAGAAAAATAAATGATCG
SP1	GAGGGCCCGAGTCAGTCAGG
CEBPZ	GTACTTTGTCATCACCAGTC

<b>TIDE</b>		
<b>MOUSE</b>	<b>Forward PCR primer</b>	<b>Reverse PCR primer</b>
<b>Mettl3_Dom1</b>	CAGAAGAGGCAGGCATCCTA	TGACTCCAGTGCTGATCGAC
<b>Mettl3_Dom2</b>	TTAGATGCACAGGGGACACA	ATGGAATTGGGCAGAGAATG
<b>HUMAN</b>	<b>Forward PCR primer</b>	<b>Reverse PCR primer</b>
<b>METTL3</b>	CTGAGGCAGGAGAATTGCTT	GGCAGCCATACACGTTAAGA
<b>METTL16</b>	GCTGAGCAAAAATCACTATGTTG	AGAGCTGTGTTTTTCAGTGTTTCA
<b>METTL1</b>	TCTGTCTCTCTTGCCGTTCTG	AGGTGCCTAGATGTCCCACAAC
<b>METTL14</b>	TCTGCAACCACTGACTGAGGAA	CCAGGAGTGATGGCTGAAATGC
<b>MOUSE</b>	<b>Forward Seq primer</b>	<b>Reverse Seq primer</b>
<b>Mettl3_Dom1</b>	CACTCTGCTGTATTTCCCATACC	TGAAAGAAGGAAAGATGACCAAA
<b>Mettl3_Dom2</b>	CCCTCTTCTCCTGTTTCTC	CCAATCTGCCCTTGTGTCTT
<b>HUMAN</b>	<b>Forward Seq primer</b>	<b>Reverse Seq primer</b>
<b>METTL3</b>	CCCAGGATTTTATCTCCATT	AGGGAAGATGACCAAATACCA
<b>METTL16</b>	TCTCCAGGACCAGCCTTCTA	TGCAGTTTGTGATGAGATGCTGT
<b>METTL1</b>	TGTCTCCGTAGCAATGCCATGA	CAACGTCAGCAGCCAGATGAAG
<b>METTL14</b>	TCTGGGTTTTTACTTGTCATGTCA	AGCATGTTAACATAAGTGCTGA

<b>shRNA sequences</b>	
METTL3 sh1	CGTCAGTATCTTGGGCAAGTTCTCGAGAACTTGCCCAAGATACTGACGTTTTTG
METTL3 sh2	GCTGCACTTCAGACGAATTATCTCGAGATAATTCGTCTGAAGTGCAGCTTTTTG
CEBPZ sh1	GATCGATTTGTATACCGAAATCTCGAGATTTTCGGTATACAAATCGATCTTTTTG
CEBPZ sh4	AGGCTACTCTTCCGCTCAAATCTCGAGATTTGAGCGGAAGAGTAGCCTTTTTTG
CTRL sh	CAACAAGATGAAGAGCACCAACTCGAGTTGGTGCTCTTCATCTTGTTGTTTTTG

<b>Cloning primers</b>	
gibSP2_fw	GCCAAAACATTAAGAAGGGCCCGATTTCAGGGGTCACTGAGCG
gibSP2_rv	GAATGGCGCTGGGCCGGCCTTGGGGGAC
gibSP1_cDNA_fw	GACGTTAACCATGAGCGACCAAGATCACTCCA
gibSP1_cDNA_rv	GTGCGTAACTCAGAAGCCATTGCCACTGATATTAATGG

<b>METTL3 mutagenesis (DW/AA mutant)</b>	
Fwd	AGTTGTGATGGCTGCCCCACCCGCGGATATTCACATGGAAGCTG
Rev	CAGTCCATGTGAATATCCGCGGGTGGGGCAGCCATCACAACT

<b>Luciferase promoter sequences</b>	
10XUAS	AGATCTGCCAAGGCGGAGTACTGTCCTCCGGGCTGGCGGAGTACTGT CCTCCGGCAAGGTCGGAGTACTGTCCTCCGACACTAGAGGTCGGAGT ACTGTCCTCCGACGCAAGGCGGAGTACTGTCCTCCGGGCTGGCGGAGT ACTGTCCTCCGGCAAGGTCGGAGTACTGTCCTCCGACACTAGAGGTCG GAGTACTGTCCTCCGACGCAAGGCGGAGTACTGTCCTCCGGGCTGGCG GAGTACTGTCCTCCGGACGCGTAGATCT
SCRAMBLED_10XUAS	AGATCTGCCAAGGTCAGGCCCTGTCCTAGGGGCTGGTCAGGCCCTGTC CTAGGGCAAGGTTCAAGGCCCTGTCCTAGGACACTAGAGGTTCAAGGCC TGTCTAGGACGCAAGGTCAGGCCCTGTCCTAGGGGCTGTCAGGCCCT GTCCTAGGGCAAGGTTCAAGGCCCTGTCCTAGGACACTAGAGGTTCAAG CCCTGTCCTAGGACGCAAGGTCAGGCCCTGTCCTAGGGGCTGGTCAGG CCCTGTCCTAGGGACGCGTAGATCT

<b>ChIP-qPCR</b>	<b>FWD</b>	<b>REV</b>
SP1 tss	TGCGTCCTTTCTGTCTCTT	AACCAATCAGAAATCAGGCG
EVI5L tss	CTCGTTATTGGGCAGAAAGC	ATAGCAAGGAAAGTGGGGGT
LRCH4 tss	CACCCAATCACAATGCTCAG	CCGTTTTCTGCTAGTGGAG
RFX1tss	TGGGAGTTGTAGTCCGCTCT	GGAGTCTTCTTTCTCGCCT
SP2 tss	ATTCAATTGGCTTTTCGGTTG	AGAGCGACGTTGATTTGACC
LMO2 tss	AAGGACCGAGAAGGAGAGG	GAGCAGGCACGAGGAGAG
HNRNPL tss	CACCAGTCACAATGACGACC	CAATCAGTGGAGACGCAGAA

<b>RT-PCR Taqman</b>	<b>FWD</b>	<b>REV</b>	<b>Probe</b>
METTL3	CGTACTACAGGATGATGGCTTTC	TTTCATCTACCCGTTTCATACCC	6
$\beta$ -ACTIN	CCAACCGCGAGAAGATGA	CCAGAGGCGTACAGGGATAG	64
DICER1	CTTAAAGTTGTTAGTGAGTGGAATGAA	CTGTTATCTATCCTGTTATCAACCAA	8
GAPDH	TCCACTGGCGTCTTCACC	GGCAGAGATGATGACCCTTTT	45
HNRNPL	TCCCCAGTTGTCCACATCA	CAAGGCCTCCACAAGGTCT	31
SP1	CAGTGGGCTACAGGGGTCT	CTTGCAATGAGCCTCCAGAT	42
SP2	CTTGTGAACGCCAGTGACA	AGTCTTAGACAGCGGGTTG	17
CEBPZ	ATAATACTAGTGAAGCCGAGAATGG	GCCAGCATAAGGTAATCTTGCT	69

<b>RT-PCR sybr green</b>	<b>FWD</b>	<b>REV</b>
Firefly Luciferase	GGCCTGACAGAAACAACCAG	AAGTCCACCACCTTAGCCTC
Renilla Luciferase	CGCTATTGTCGAGGGAGCTA	GCTCCACGAAGCTCTTGATG