Supplementary Figures

Figure S1

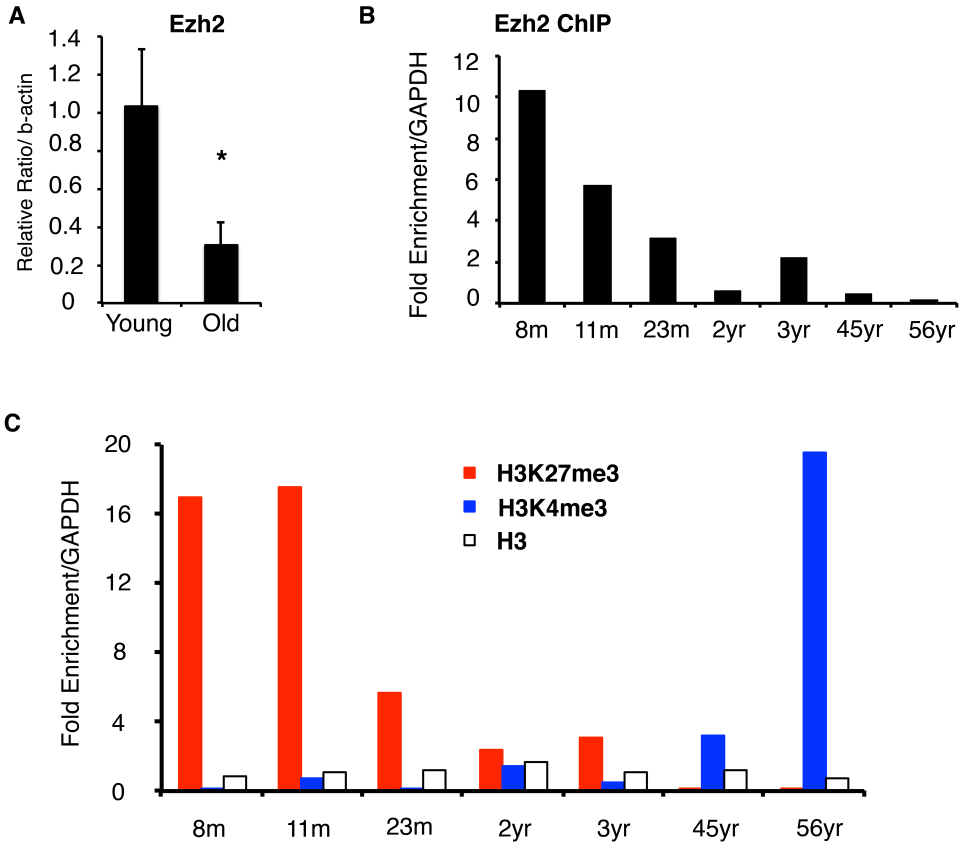

Figure S1. Loss of Ezh2 in aging human islets

(**A**) Ezh2 mRNA level in young (<20 yrs) and old (20 yrs+) human islets. (**B**) ChIP analysis of Ezh2 binding to the *Ink4a* locus in human islets (8 months, 11 months, 23 months, 2 years, 3 years, 45 years and 56 years old). (**C**) ChIP analysis of histone modifications (H3K4me3 in green, H3K27me3 in red) in human islets as in (**B**). *$p < 0.05$

Figure S2

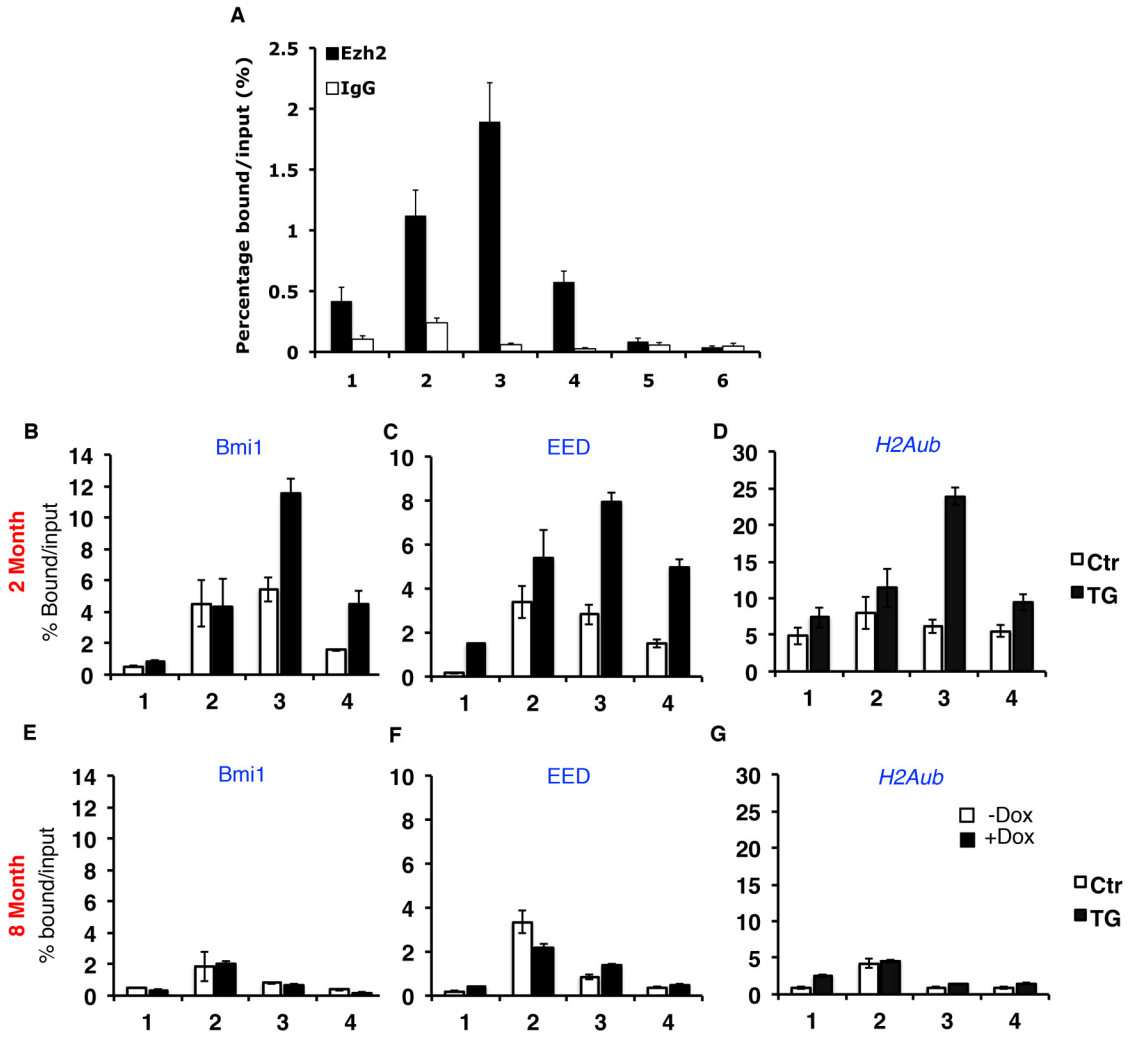

Figure S2. Ectopically expressed Ezh2 recruited other PRC members in 2-month bEzTG islets but not 8-month

(**A**) ChIP analysis for Ezh2 antibody, along with control IgG, in islets from 6 weeks old, wild-type mice, at the *Ink4a* locus (primer pairs 1-4), along with control primer pairs 5 (GAPDH promoter) and 6 (beta actin), showing specific recruitment at the *Ink4a* locus. (**B-G**) Representative ChIP analysis for the indicated antibody at the *Ink4a* locus in islets isolated from 2 month (**B-D**) and 8 month (**E-G**) old age groups.

Figure S3

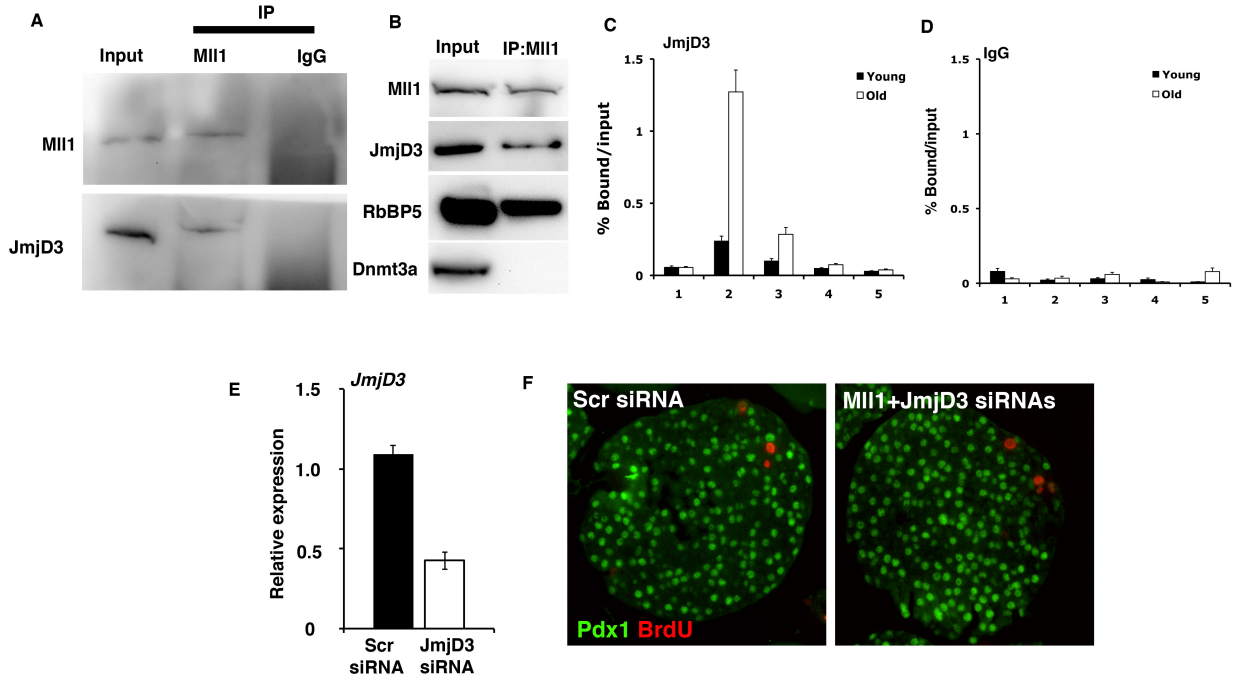

Figure S3. JmjD3 interacts with Mll1 complex and associates with *Ink4a* locus in an age dependent fashion in mouse islets.

(**A, B**) Cell extracts from Min6 cells were used for IP with an anti-Mll1 antibody or IgG and analyzed by immuno-blotting with indicated antibodies. **(C, D)** Representative ChIP results for the indicated antibody (JmjD3 and control IgG) at the *Ink4a* locus (primer sets 1-4), or negative control HoxC13B (primer set 5), in islets from young and old mice. **(E)** Relative *JmjD3* mRNA expression levels as shown by real-time PCR in islets from old mice treated either with siRNA targeting *JmjD3*, or a control, scrambled (Scr) siRNA . (**F**) Islets from 2 months old mice were treated either with scrambled (Scr) siRNA or a combination of siRNAs targeting *Mll1* and *JmjD3*, and islets sections were immunostained for BrdU (red) and Pdx1 (green), showing no change in islet proliferation upon knockdown of *Mll1* and *JmjD3* in islets from young mice.n=3 experiments (20X magnification).

Figure S4

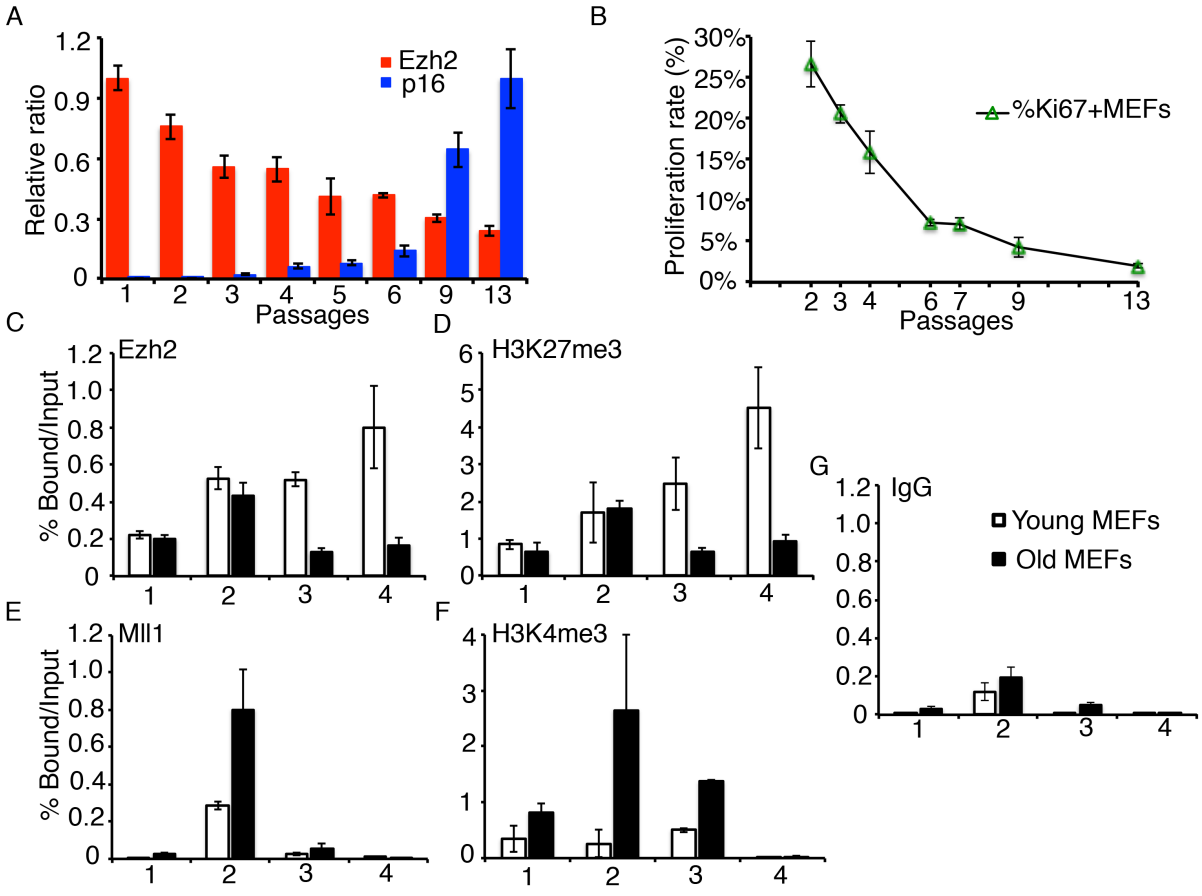

Figure S4. Serial-passaged MEFs are associated with increased p16ink4a regulated by PcG-TrxG on the *Ink4a* locus

(**A**) Real time qRT-PCR showing p16ink4a increases with passages while Ezh2 declines. (**B**) Proliferations deceased as we passaged the MEFs. (**C-G**) ChIP analysis for the indicated antibody at the *Ink4a/Arf* locus in MEFs showing decreased Ezh2 and H3K27me3 and increased Mll1 and H3k4me3 in old MEFs. n=3 experiments.

Supplementary materials

Table S1. RT-PCR primers

Gene	Forward	Reverse
Myc-Ezh2	5'-TTTCTGACGATTGGAACTAAACATAG-3'	5'-TTTCTGACGATTGGAACTAAACATAG-3'
Ezh-2	5'-TGTAGACAGGTGTATGAGTTTAGAG-3'	5'-GGTCAGCAGCTCCACACGTGAGAC-3'
Ink4a	5'-ATCTGGAGCAGCATGGAGTC-3'	5'-CTGAGGCGGATTTAGCTCTG-3'
Tubulin	5'-GTTGGCCAGGCTGGTGTCCAG-3'	5'-CTGTGATGAGCTGCTCAGGGTGG-3'

Table S2. Real-time qRT-PCR primers

Gene	Forward	Reverse
Mll-1	5'- AGCAGCTCTCATTTGCAGGT -3'	5'- ACAACGGCATCATGGAGAAT -3'
Ezh-2	5'-TGGAAGCAGCGGAGGATA-3'	5'-GTCACTGGTGACTGAACACTCC-3'
JmjD3	5'- CTGTACAGACCCCCGGAAC-3'	5'-TGGTGGAGAAAAGGCCTAAGT -3'
Ink4a	5'- CCGTGTGCATGACGTGCGGG -3'	5'-GCTGCTACGTGAACGTTGCCC -3'
Cyclophilin	5'-GTTGGCCAGGCTGGTGTCCAG-3'	5'-CTGTGATGAGCTGCTCAGGGTGG-3'