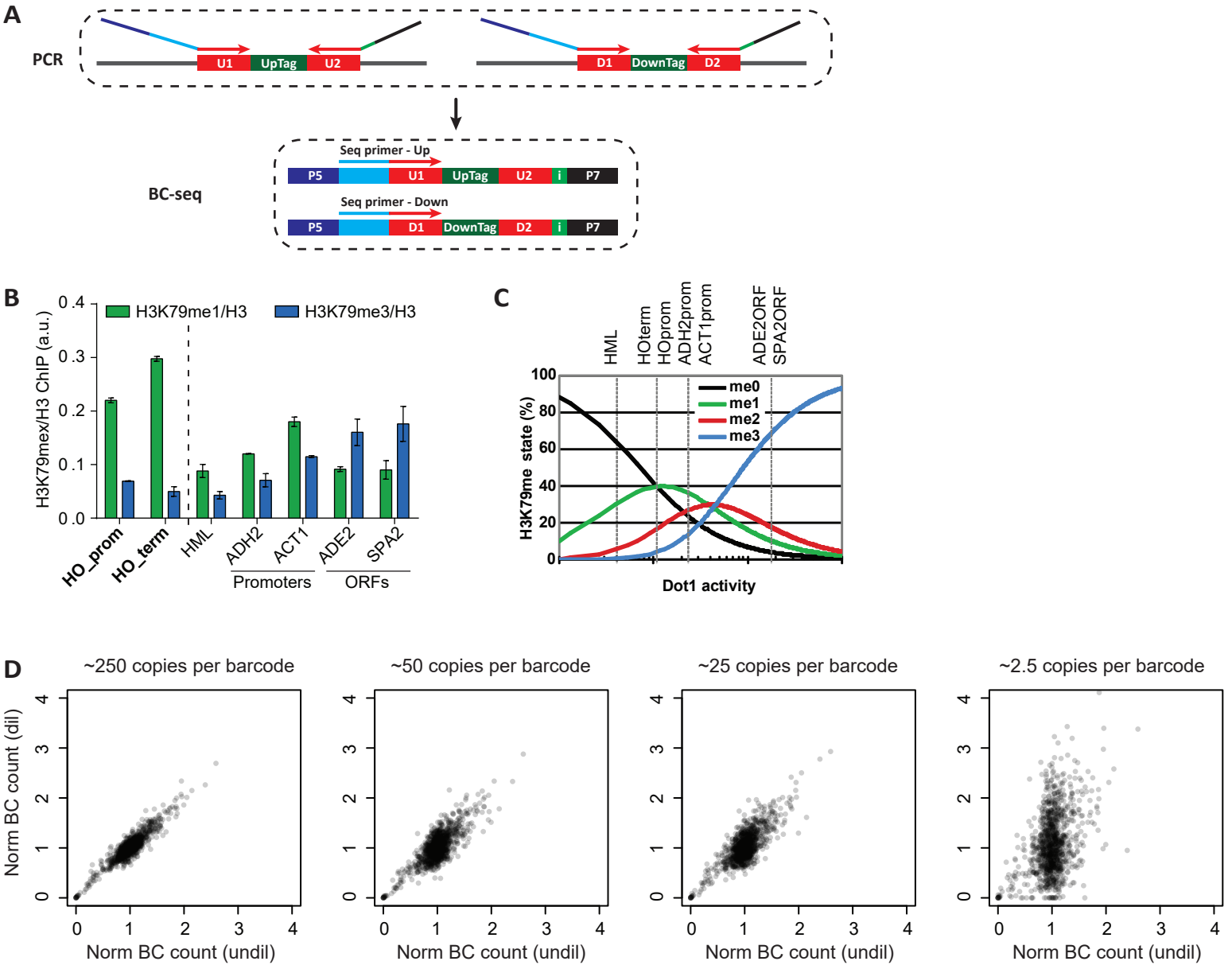

Figure 1 -figure supplement 1. Technical details on Epi-ID.

A) PCR set-up, introducing sequencing adapters and an index in a single PCR. Two custom sequencing primers were designed to include the U1/D1 sequence just upstream of the UpTag and DownTag. Starting the reads with the barcode yields maximum complexity in the first base pairs, which is good for clustering efficiency. These sequencing primers are compatible with standard Illumina sequencing conditions and can be mixed together to sequence UpTag and DownTag in one lane. A 6-base-pair index is introduced in the reverse primer, to allow for multiplexing. B) ChIP-qPCR data of the different methylation states, normalized to H3, at several loci. HO promoter and HO terminator are near the UpTag and DownTag, respectively. Error bars show the range of two biological replicates. C) Dependence of H3K79me levels on Dot1 activity, modified from De Vos et al. (2011). Although this is a model based on global H3K79 methylation, qualitatively similar changes in methylation can be expected on lowly versus highly methylated loci. Dashed lines indicate estimated levels of H3K79 methylation at the loci tested in the qPCR. HML, a silent mating type locus, has very low levels of methylation, the two promoters have intermediate levels and the two ORFs have high levels of methylation. HO promoter and HO terminator have a low to intermediate level of H3K79 methylation, both an increase and a decrease of methylation are possible, making these loci suitable for a regulator screen. D) It is important to start the PCR with sufficient material to minimize jackpot effects. Scatter plots showing the correlation between barcode counts after a PCR starting with approximately 2500 copies per barcode (on the x axis), with barcode counts of PCRs on diluted sample. The correlation decreases with dilution, 250 copies per barcode seems to be sufficient to have minimal jackpot effect.