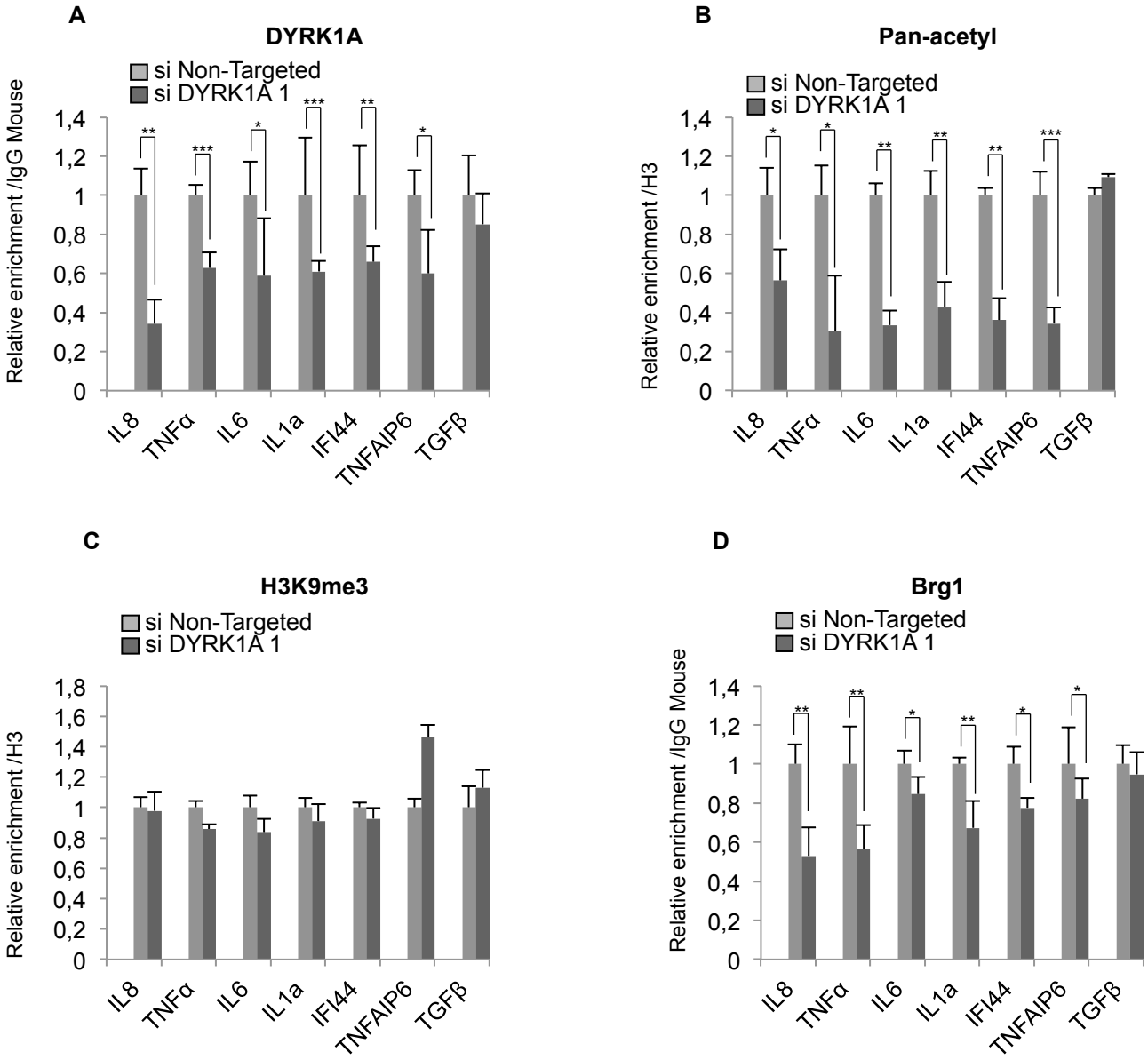
A
DYRK1A
si Non-Targeted
si DYRK1A 1
Relative enrichment /IgG Mouse
1,4
1,2
1
0,8
0,6
0,4
0,2
0
IL8
TNFα
IL6
IL1a
IFI44
TNFAIP6
TGFβ
B
Pan-acetyl
si Non-Targeted
si DYRK1A 1
Relative enrichment /H3
C
H3K9me3
si Non-Targeted
si DYRK1A 1
Relative enrichment /H3
1,8
1,6
D
Brg1
si Non-Targeted
si DYRK1A 1
Relative enrichment /IgG Mouse

E

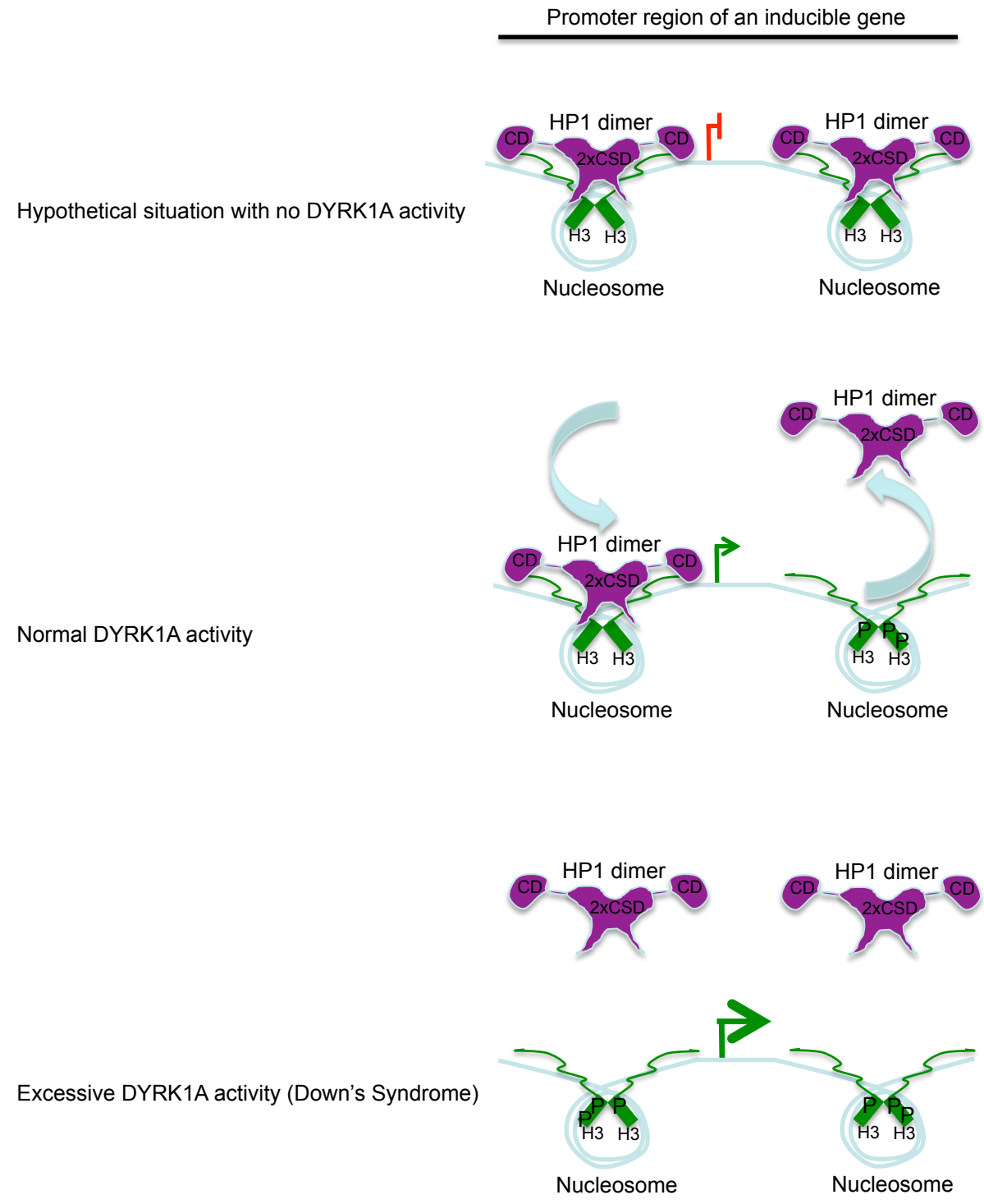
Promoter region of an inducible gene
Hypothetical situation with no DYRK1A activity
HP1 dimer
CD
2xCSD
H3
Nucleosome
Normal DYRK1A activity
Excessive DYRK1A activity (Down's Syndrome)
P

Fig S3. Depletion of DYRK1A antagonizes open chromatin marks at inducible genes – Additional ChIPs and Model. (**A**–**D**) HeLa cells were transfected with either non-targeted or DYRK1A siRNAs. Accumulation of the indicated proteins or histone modifications at the promoter of the list genes was evaluated by ChIP analysis followed by qPCR. Data are normalized to the values obtained with either non-immune IgGs or anti-histone H3 antibodies as indicated. Data shown are means +/- SEM from three independent experiments. In each panel, significance of the differences was estimated using Student's *t*-test (***: $p<0.001$; **: $0.001<p<0.01$; *: $0.01<p<0.05$). (**E**) Model for transcriptional regulation of inducible genes by DYRK1A and HP1 proteins. At normal levels of DYRK1A expression, limited phosphorylation at H3T45 and H3S57 interferes with H3-HP1 interaction and imposes a labile and dynamic recruitment of the HP1 proteins to the promoter that in turn allows for expression of the downstream gene at a moderate level. Under conditions where DYRK1A activity is reduced (for example, after its depletion with siRNAs), HP1 binding to the promoter region is no longer hindered and transcription is repressed. Inversely, increased levels of DYRK1A (as observed in the megakaryoblastic leukemia cells from Down's Syndrome patients) increased phosphorylation at H3T45 and H3S57 strongly inhibits HP1 recruitment and results in chronic transcriptional activity of several genes involved in innate immunity and cell cycle regulation. The additional layer of complexity added by the differential binding of the three HP1 isoforms to H3T45p and H3S57p is not depicted in this model. In the schematic, nucleosomes are represented only by the two turns of DNA, and the histone H3 tail and first helix.