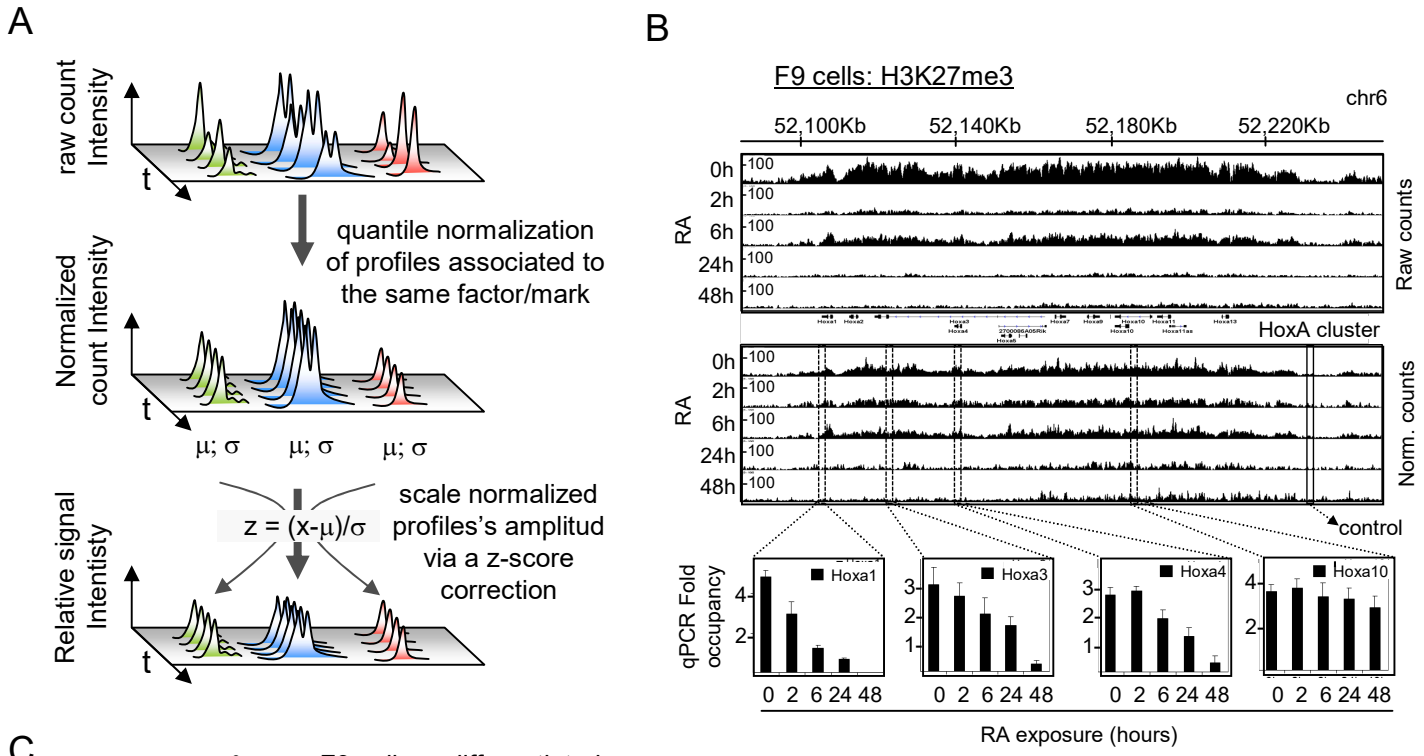

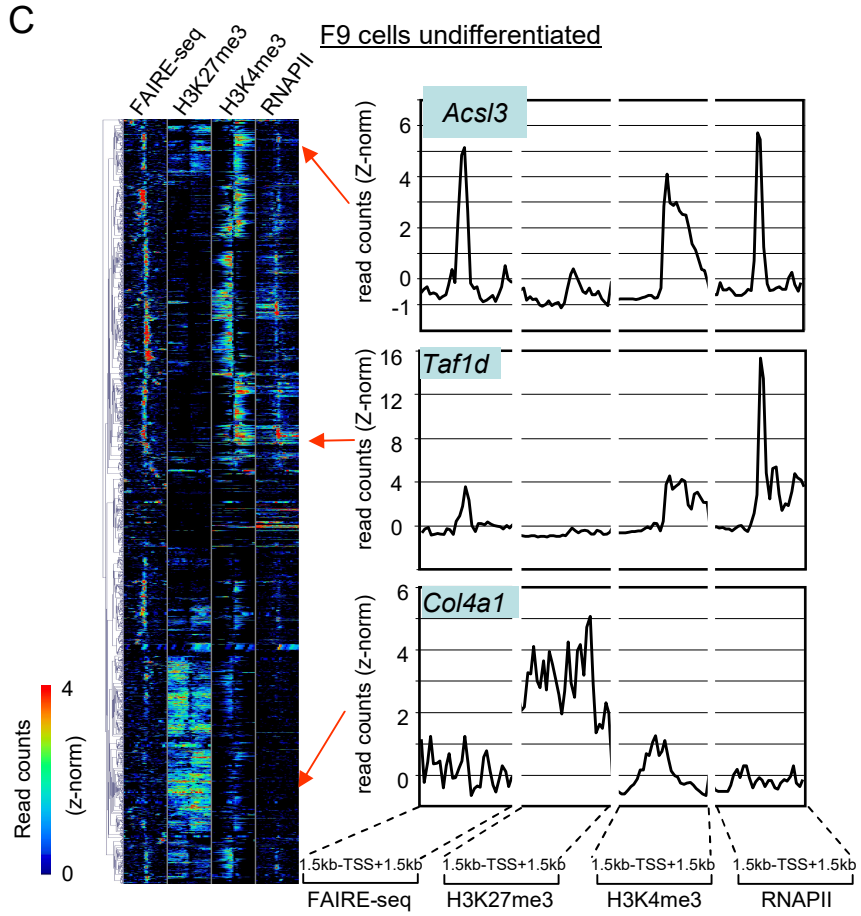

Supplemental Figure S5. Two-step normalization procedure for multi-profile comparisons. (A) Technical variation resulting for example from different antibody affinities/efficacies or sequencing depth directly influence the enrichment amplitudes in ChIP-seq assays. To compare assays we have developed Epimetheus, a two-step normalization procedure in which (i) the raw count intensity in ChIP-seq datasets produced with antibodies targeting the same factor are corrected following quantile normalization and (ii) normalized read-counts are brought to the same scale via z-score normalization. **(B)** Illustration of the effect of quantile normalization on H3K27me3 datasets from different time-points during RA-induced F9 differentiation. Note that the 2h dataset displayed lower intensity levels in the HoxA cluster relative to the 6h profile; after quantile correction, the 2h dataset becomes similar to the 0h dataset. This last observation has been confirmed by qPCR measurements at various genomic regions covering the HoxA cluster **(C)** Example of the z-score scaling correction applied to normalized datasets corresponding to the chromatin accessibility FAIRE-seq profile, the 'repressive' H3K27me3 and the 'active' H3K4me3 marks, and RNA polymerase II (RNAPII). The enrichment levels of these factors around the promoter (± 1.5kb) of genes participating at the RA-induced F9 differentiation process are displayed (left panel, heatmap). The right panel depicts 3 examples of promoter regions in which FAIRE, H3K4me3 and RNAPII are preferentially enriched (*Acsl3*, *Taf1d*) and correlate with an active gene transcription, in contrast to the preferential enrichment of H3K27me3 at the *Col4a1* promoter, which is indicates repression.