# **Supplementary Methods**

## DNA methylation analysis by Illumina Methylation Arrays

For human and mouse data, β-values were calculated representing the percentage of DNA methylation at a certain cytosine base. Prior analysis, rs loci, loci on gonosomes and loci with a detection p-value > 0.01 were excluded from further analysis. Furthermore, a cut-off for the loci call rate at 95% was set. Duplicates were merged by calculating the mean DNA methylation.

## Segmentation of chromatin states in human and in mice

For analysis of murine data, publicly available chromatin immunoprecipitation DNA-sequencing (ChIP-Seq) data for the marks H3K27ac, H3K27me3, H3K4me1, H3K4me3 and H3K36me3 from spleen and thymus from 8 weeks old mice were obtained from ENCODE (Lab: Bing Ren, UCSD, Table S4).1 Using these data, the mouse genome was segmented into a ten-state combinatorial chromatin model and then collapsed into five functional chromatin states (Table S5), summarizing similar states based on emission probabilities as described in Kretzmer et al.2 Segmentation using the ChIP-Seq data for the five histone modifications was done with the ChromHMM software (version 1.24).3

## Bioinformatic and statistical analyses

The epigenetic age was determined through the Horvath clock utilizing the methylclock package (version 1.6.0).4 The proliferation history was analyzed using the epiCMIT tool.5 Gene ontology enrichment analysis was performed using the EnrichR webtool (https://maayanlab.cloud/Enrichr/). As background, genes found on both, the human and murine Illumina BeadChip array, were used. Heatmap representation was done with the ComplexHeatmap package (version 2.16.0).6 To study CpGs dynamically methylated during B-cell development, the 93,851 CpGs allocated by Kulis et al. to 20 Kulis modules (M1-M20) were interrogated, from which 86,957 CpGs overlap with the 441,870 CpGs that passed the quality assessment.7

## References

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