Supplementary Figure 1

The induction and effect of c-Maf on CD4+ T cell differentiation in vitro.

a. Naive CD4+ T cells from Maf<sup>fl/fl</sup> and Maf<sup>fl/fl</sup>Cd4-cre were sorted and stimulated in vitro with anti-CD3 and anti-CD28 in the presence of medium alone, IL-12, IL-27, IL-12+IL-27, IL-4, TGF-β+IL-6 or TGF-β and assessed for the mRNA expression of Maf, Il10 and master regulator transcription factors Tbx21, Gata3, Rorc and Foxp3 and hallmark cytokines Ifng, Il4 and Il17a as well as Il2ra relative to Hprt as follows. Medium, IL-12, IL-27, IL-12+IL-27: Maf, Il10, Tbx21, Ifng (day 3); IL-4: Maf (day 5), Il10 (day 5), Gata3 (day 4), Il4 (day 5); TGF-β+IL-6: Maf (day 1), Il10 (day 2), Il17a (day 5); TGF-β: Maf, Il10, Foxp3, Il2ra (day 3) (n=3 culture wells per condition, mean±SD; * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001, unpaired t-test, two-tailed). Representative data from three biological experiments are shown.

b. Naive CD4+ T cells from wild-type mice were sorted, stimulated as in (a) and assessed for intracellular c-Maf on day 3. Depicted are dot plots of c-Maf versus isotype control gated on live CD4+ T cells. Representative data from two independent experiments are shown.
Supplementary Figure 2

Supporting information for differential gene expression analyses.

CD4+ T cells from malaria, HDM and EAE challenged Maffl/fl Cd4-cre vs Maffl/fl mice were profiled by RNA-seq. a, Volcano plots of differentially expressed genes, with previously associated regulators of IL-10 depicted (blue, significantly down-regulated; red, significantly up-regulated; grey, non-differentially expressed) (n=3 independent animals (malaria) or biologically independent samples (HDM and EAE) per genotype; P < 0.05, absolute FC ≥ 1.5, moderated t-test, two-tailed). b, Manually curated list of top biological pathways as determined by GO enrichment analysis of each differentially up- and down-regulated genes in Maffl/fl Cd4-cre vs Maffl/fl mice (n=3 independent animals (malaria) or biologically independent samples (HDM and EAE) per genotype).
Supplementary Figure 3

Effect on pathology and phenotype of $T_{FH}$ cells in acute phase of malaria.

a. Schematic of $P$. chabaudi infection in $Bcl6^{fl/fl}$ and $Bcl6^{fl/fl}; Cd4$-cre mice, percentage weight loss (n=5, mean±SD) and temperature changes (n=8, mean±SD) on day 9 post $P$. chabaudi infection. Representative data from two biological experiments are shown. b. Representative cytokine staining of CD4$^+$ T cells on day 14 post $P$. chabaudi infection in C57BL/6/J mice, plots are gated on live CD3$^+$CD4$^+$CD44$^+$ T cells. Pooled data from two biological experiments are shown (n=5, mean±SD).
Supplementary Figure 4

Changes in chromatin accessibility do not account for transcriptional disregulation in the absence of c-Maf.

Volcano plots of accessibility changes in ATAC-Seq consensus peak sets in CD4+ T cells from malaria, HDM allergy and EAE challenged Maf<sup>fl/fl</sup>Cd4-cre vs Maf<sup>fl/fl</sup> mice (n=3 independent animals (malaria) or biologically independent samples (HDM and EAE) per genotype, statistical significance called using DiffBind 2.02 with FDR < 0.05, absolute fold change ≥ 1.5) assigned to genes (see Supplementary Information for computational methods) and mapped to RNA-seq fold-change values. The top ten peaks ranked by fold-change were labeled with their assigned gene, as well as any remodeled peak assigned to Il10.
Supplementary Figure 5

Framework schematic for the identification of putative direct targets of c-Maf.

For each disease model, the c-Maf ChIP-seq (GSE40918) and motif datasets were filtered according to the accessibility as determined by ATAC-seq, allowing the identification of putative c-Maf binding sites and estimation of its relevance in explaining RNA-seq-defined transcriptional changes observed upon c-Maf deletion (see Supplementary Information for computational methods).
Supplementary Figure 6

Genome browser tracks of other key immune genes.

Genome browser tracks of read coverage of RNA-seq and ATAC-seq in CD4+ T cells from the malaria, HDM allergy and EAE challenged $\text{Maf}^{fl/fl}\text{Cd4-cre}$ vs $\text{Maf}^{fl/fl}$ mice (shown as an overlay of n=3 independent animals (malaria) or biologically independent samples (HDM and EAE) per genotype), as compared to untreated control and matched to c-Maf ChIP-seq (GSE40918) and motif sites.