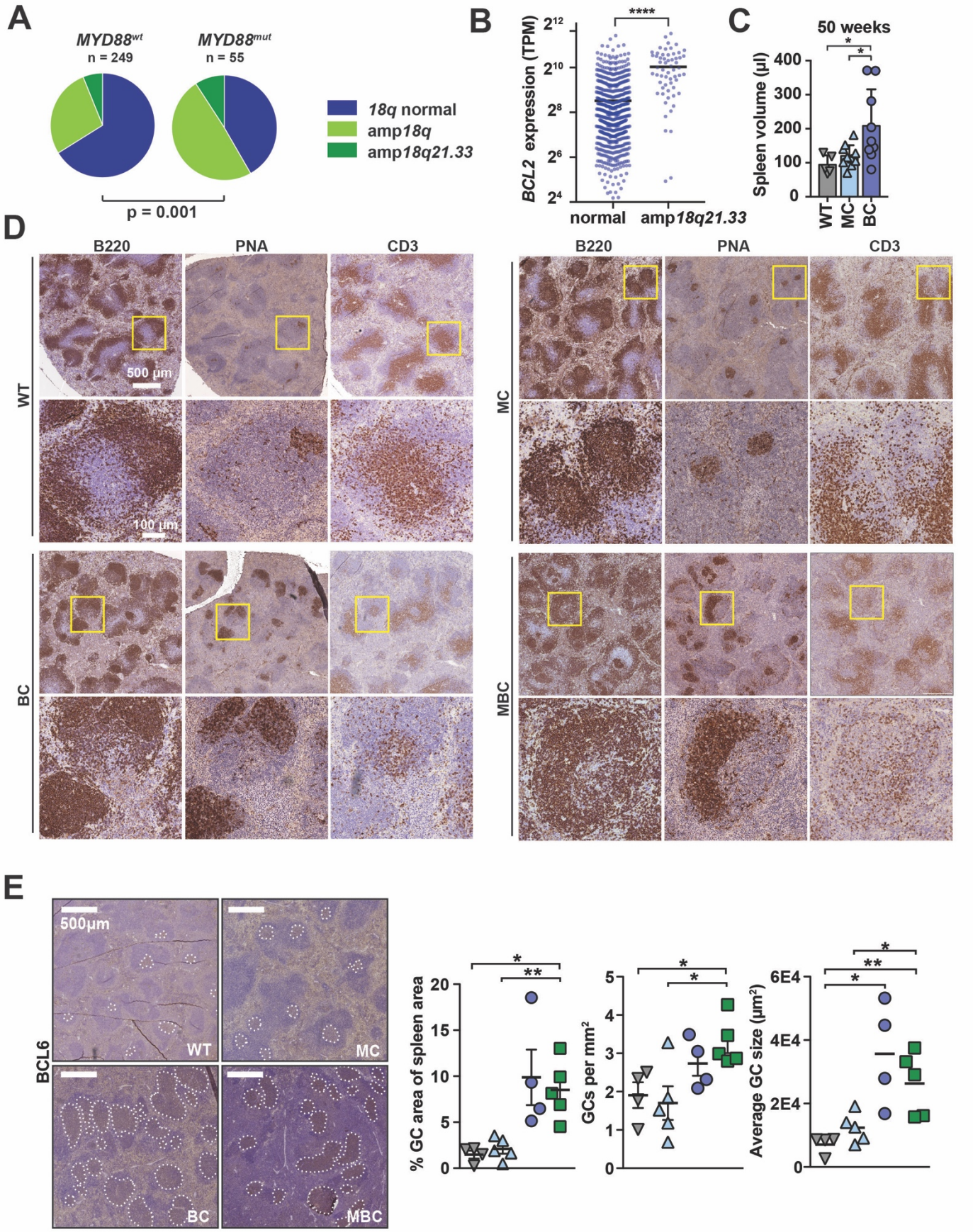
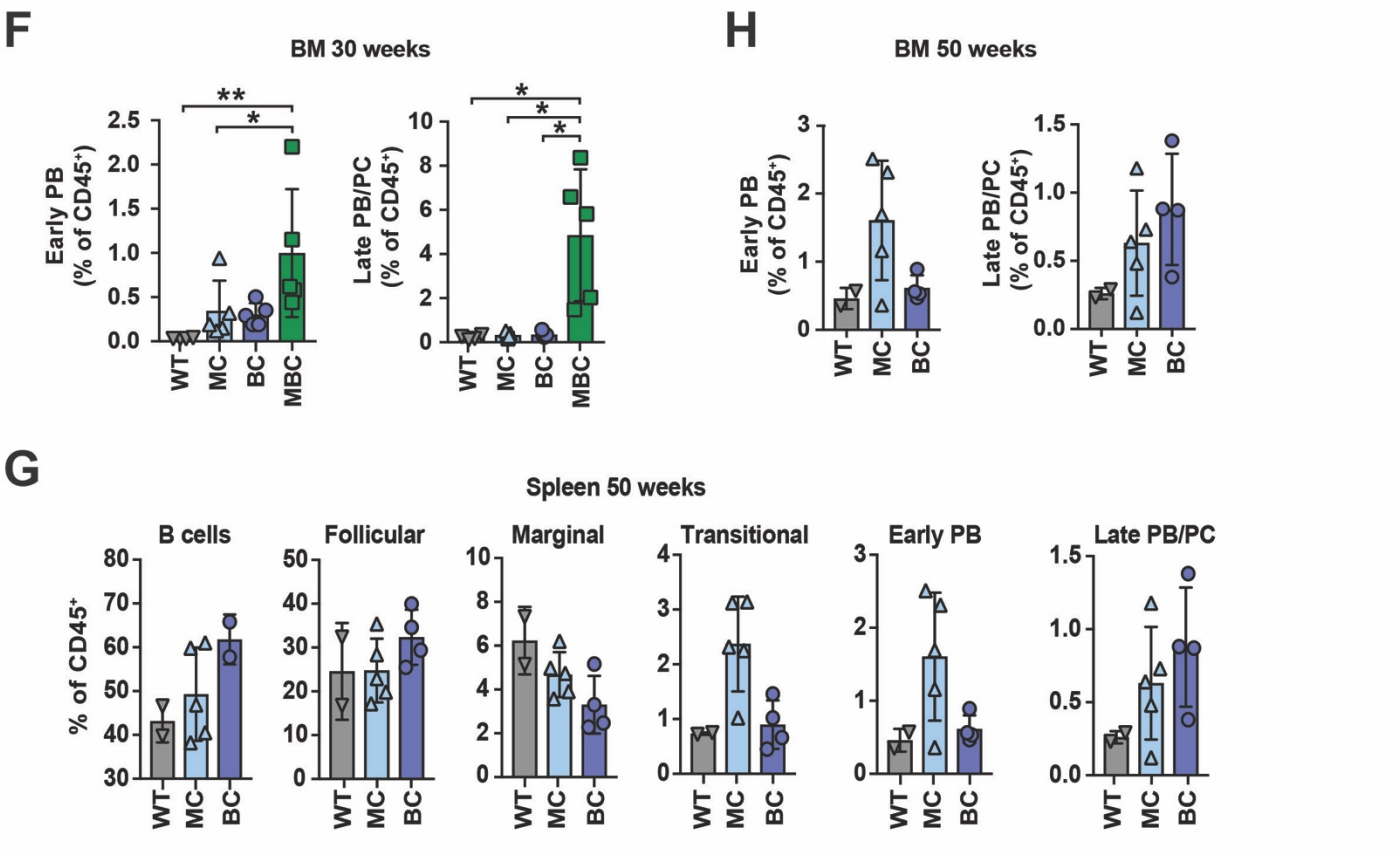
Flümann et al., Supplementary Figure 1

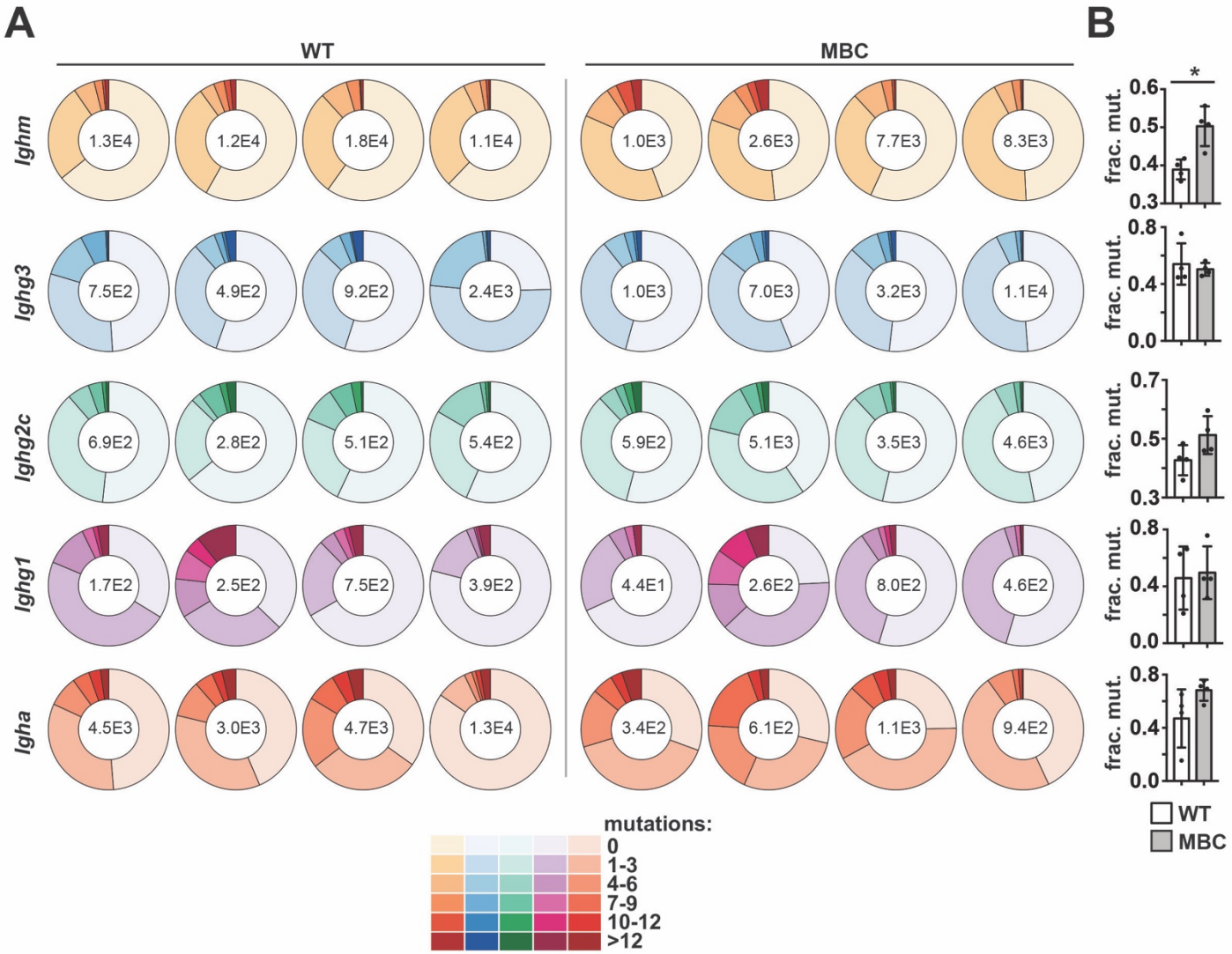


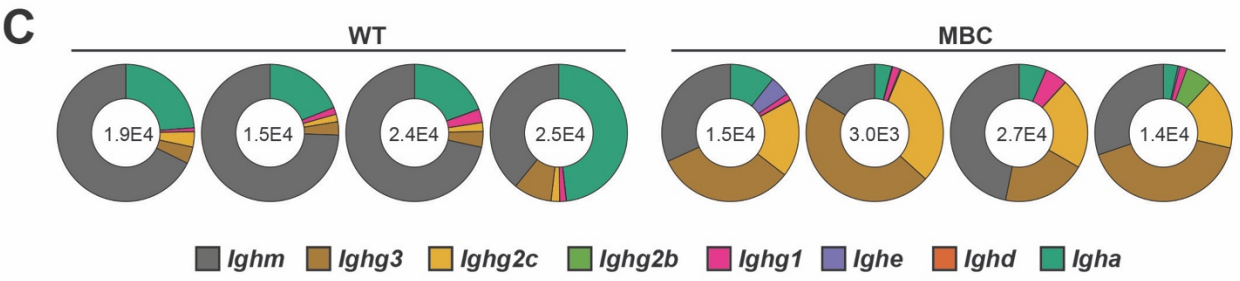
Flümann et al., Supplementary Figure 1

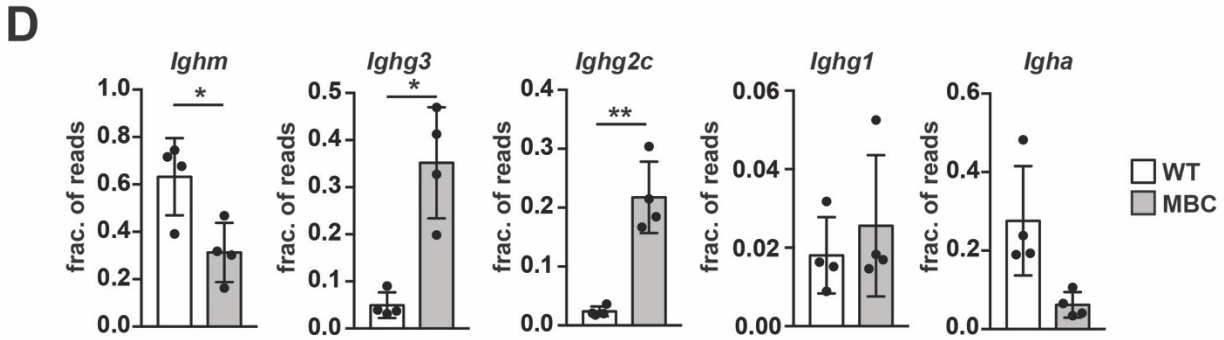


Supplementary Figure 1 - A) The *BCL2* amplification status of *MYD88* wt and mutant samples was analyzed in a published dataset (9). The statistical analysis compared *BCL2*^{amp} cases (presence of a *18q* or *18q21.33* amplification) to *18q* wt cases. **B)** A publicly available dataset (11) was analyzed for *BCL2* expression with respect to the *BCL2* amplification status. **C)** Spleen volumina of 50 weeks old wt (n = 5), MC (n = 9) and BC (n = 9) animals were determined by MR imaging. **D)** Exemplary immunohistochemical stainings for B220, CD3 and PNA of splenic sections of 30 weeks old WT, MC, BC and MBC animals. **E)** Germinal center structures were visualized by immunohistochemical staining for BCL6 on splenic sections of WT, MC, BC and MBC animals and quantified. **F)** Flow cytometric analysis of bone marrow cells from 30 weeks old animals for early plasmablasts (PB, B220^{+}, MHCII^{+}, CD138^{+}) and late PB/plasma cells (B220-/MHCII-, CD138^{+}). **(G)** Splenocytes of 50 weeks old wt, MC and BC animals were analyzed by flow cytometry. **H)** Flow cytometric analysis of bone marrow cells from 30 weeks old animals. *, $p \leq 0.05$; **, $p \leq 0.01$; ****, $p \leq 0.0001$. A) Fisher's exact test. B-F) Welch's unpaired two-tailed t-test.

Flümann et al., Supplementary Figure 2

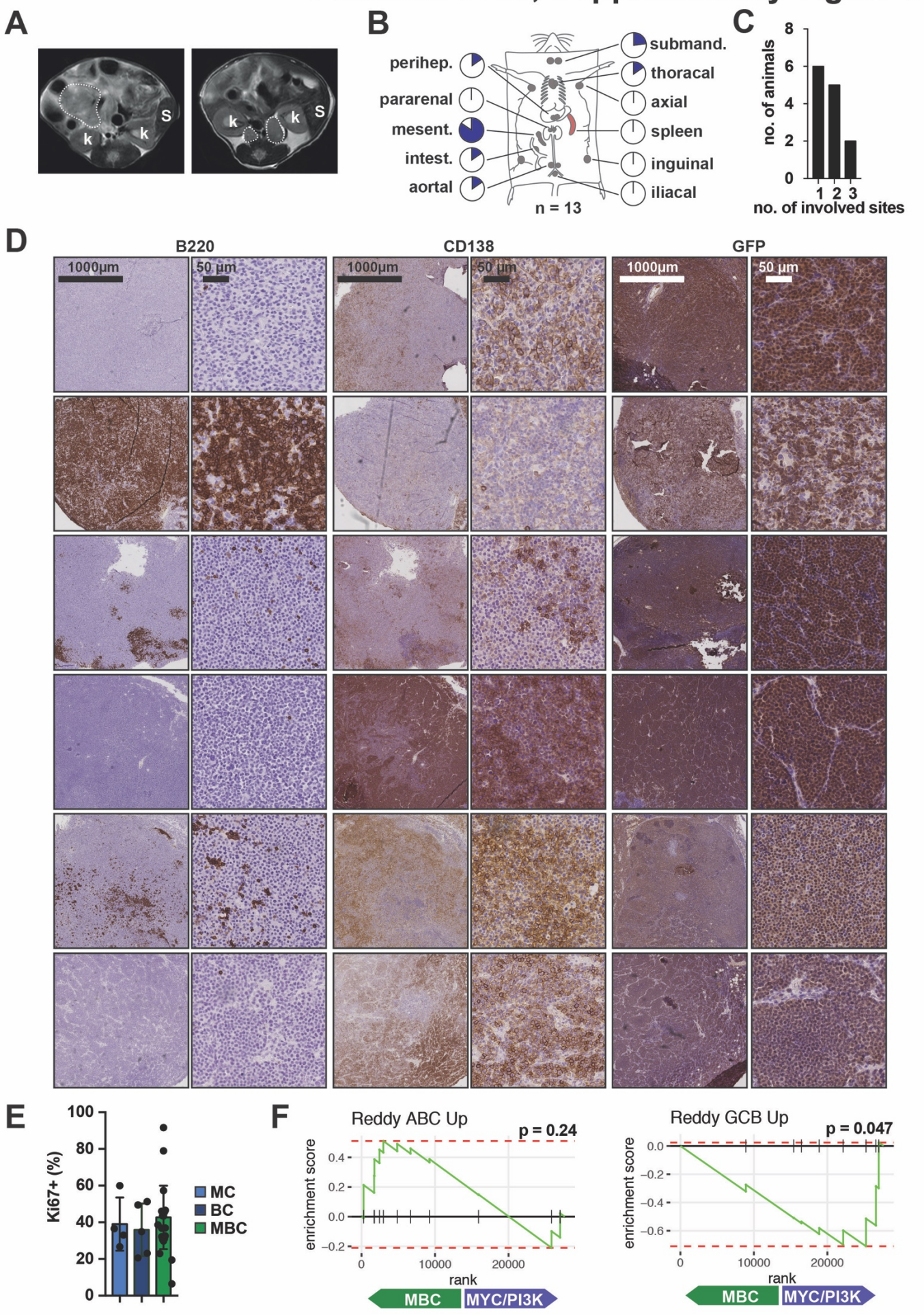




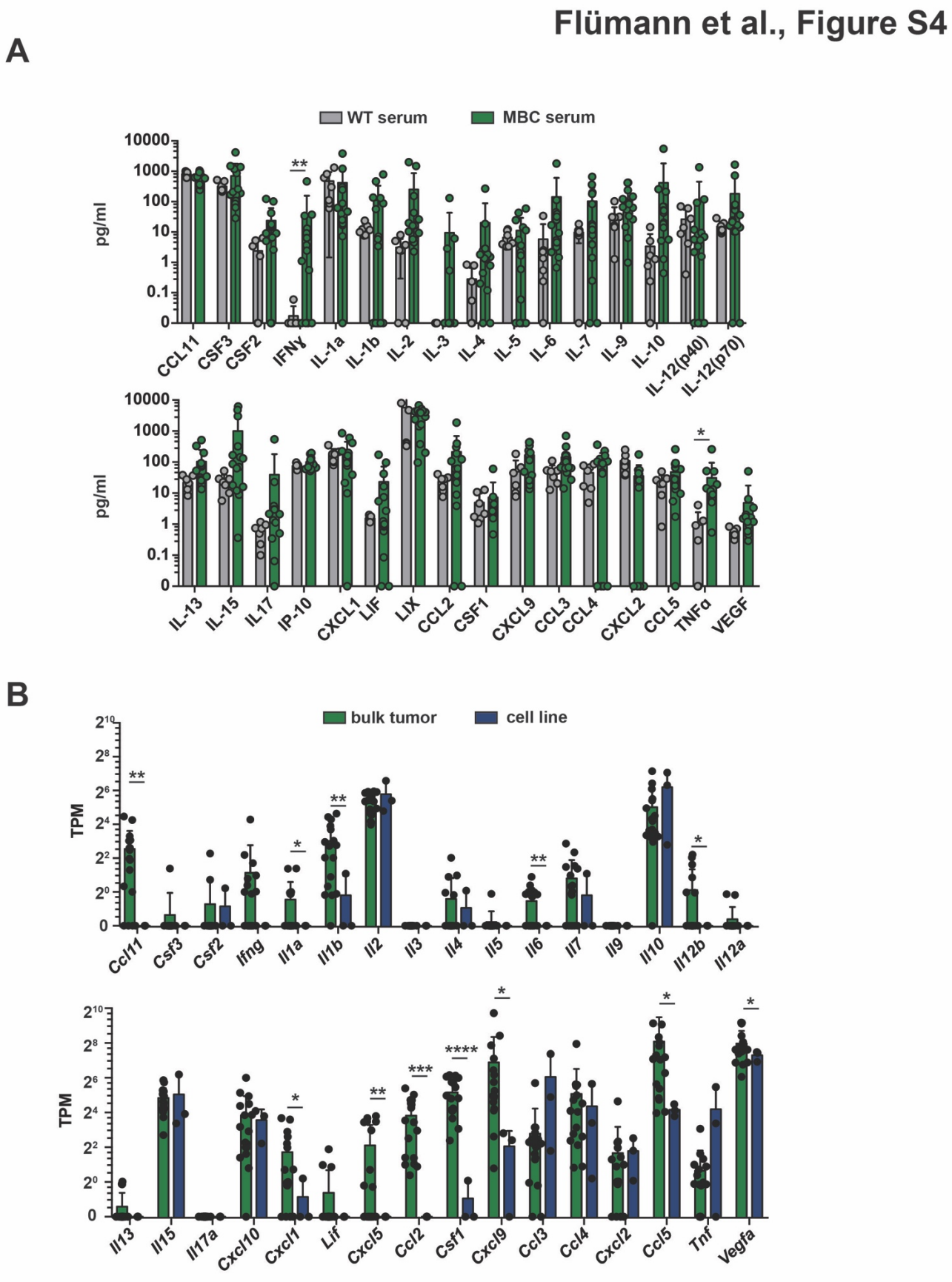


Supplementary Figure 2 – $CD138^+$ cells were isolated from spleens of 10 weeks old wt and MBC animals (n = 4 per genotype) and full-length BCR repertoire sequencing was performed (21). **A)** Constant region-specific frequencies of clones with 0, 1-3, 4-6, 7-9, 10-12 or >12 mutations in the V(D)J region. Each column represents one animal, the total number of sequences (i.e. MIGs) for each isotype is given for each sample. **B)** Frequencies of germline and mutated V(D)J sequences. **C)** Distribution of constant regions for each sample. The total number of MIGs per sample is given. **D)** Frequencies of clones with *Ighm*, *Ighg3*, *Ighg2c*, *Ighg1*, *Igha* constant regions for wt and MBC samples. *, $p \leq 0.05$; **, $p \leq 0.01$, Welch's unpaired two-tailed t-test.

Flümann et al., Supplementary Figure 3

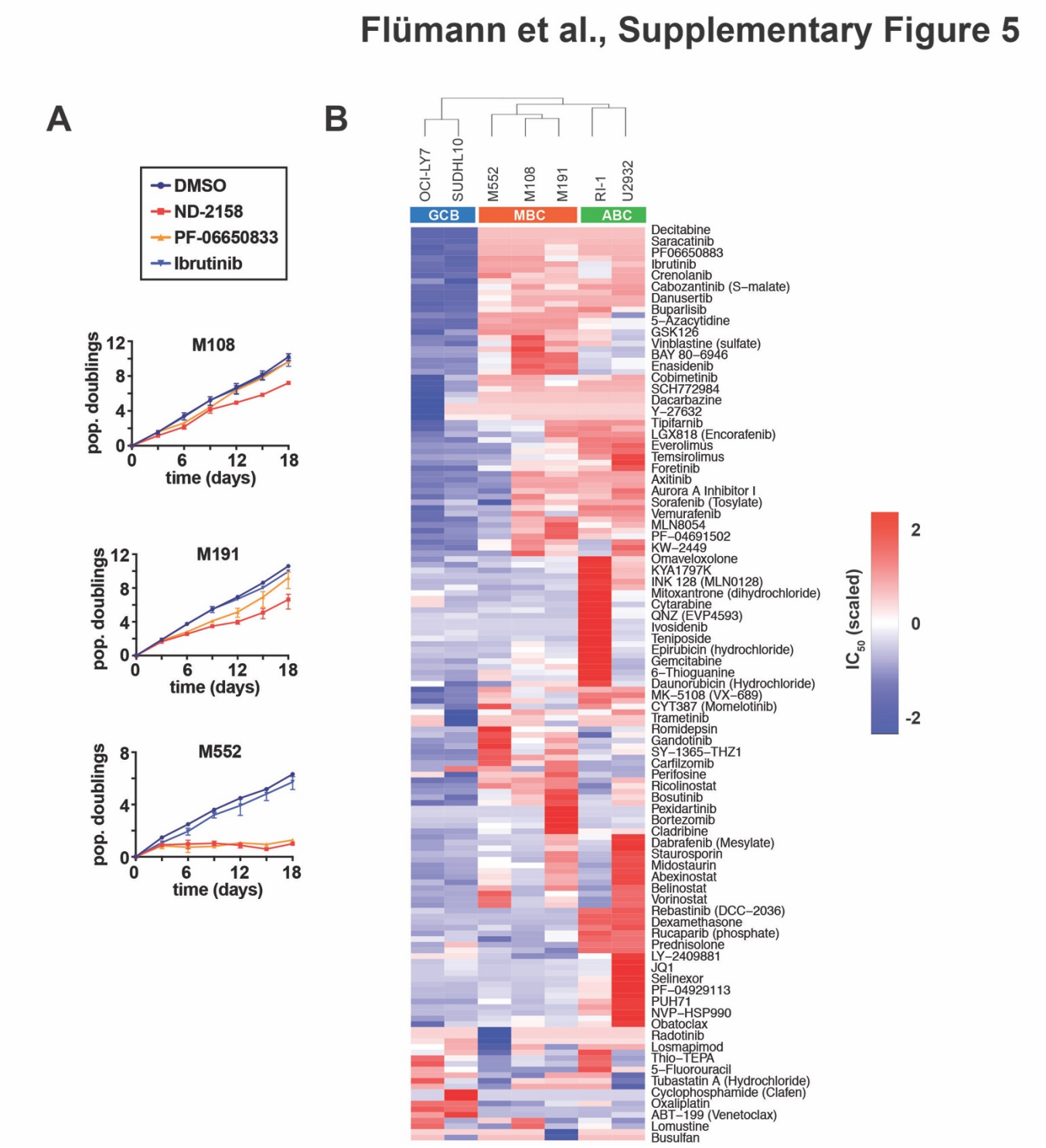


Supplementary Figure 3 – A) MR images of two animals harboring tumors at the most frequent sites of location, the mesenterial area (left) or retrorenal (right). Tumors are outlined by dashed lines. k, kidney; s, spleen). **B)** Localization of lesions in 13 MBC animals. Lymph nodes (LN) were considered involved if their diameter exceeded 7mm, the threshold for splenic involvement was a weight of more than 450mg. **C)** Number of distinct involved sites of 13 MBC animals. **D)** 6 lesions from individual MBC animals were stained for B220, CD138 and GFP. **E)** Quantification of the percentage of Ki67-positive cells in tumors of MC (n = 4), BC (n = 5) and MBC (n = 19) mice. **F)** Gene set enrichment analysis for published ABC and GCB gene sets comparing 3 MBC tumor-derived cell lines to six cell lines derived from *R26*$^{LSL.MYC/LSL.P110*}$*;Cg1-Cre* tumors.



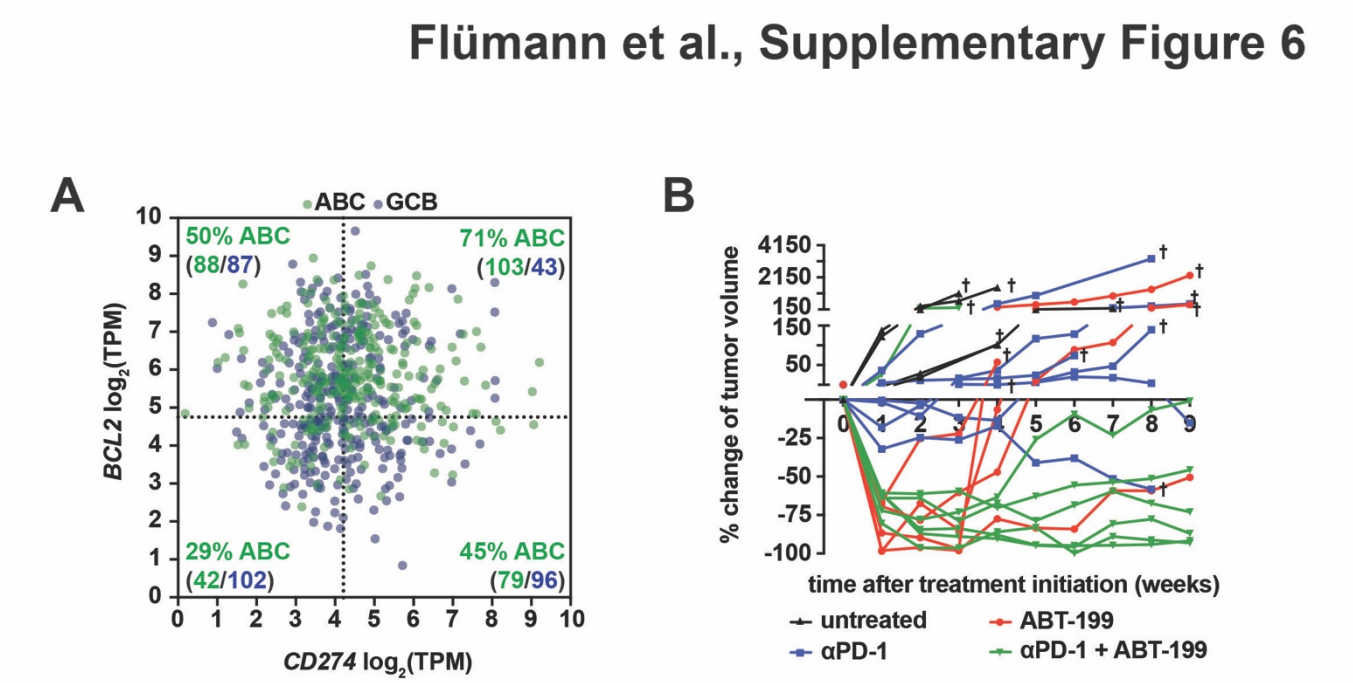
Supplementary Figure 4 – A) Alternative representation of the data set in **Fig. 4J**. Cytokine levels in the sera of lymphoma-bearing MBC animals (n = 15) were measured and compared to

wt levels (n = 7). **B)** Comparison of cytokine expression levels in 3'RNA sequencing profiles between MBC bulk tumors (n = 17) and MBC tumor-derived stable cell lines (n = 3). *, $p \leq 0.05$; **, $p \leq 0.01$; ***, $p \leq 0.001$; ****, $p \leq 0.001$, Welch's unpaired two-tailed t-test.

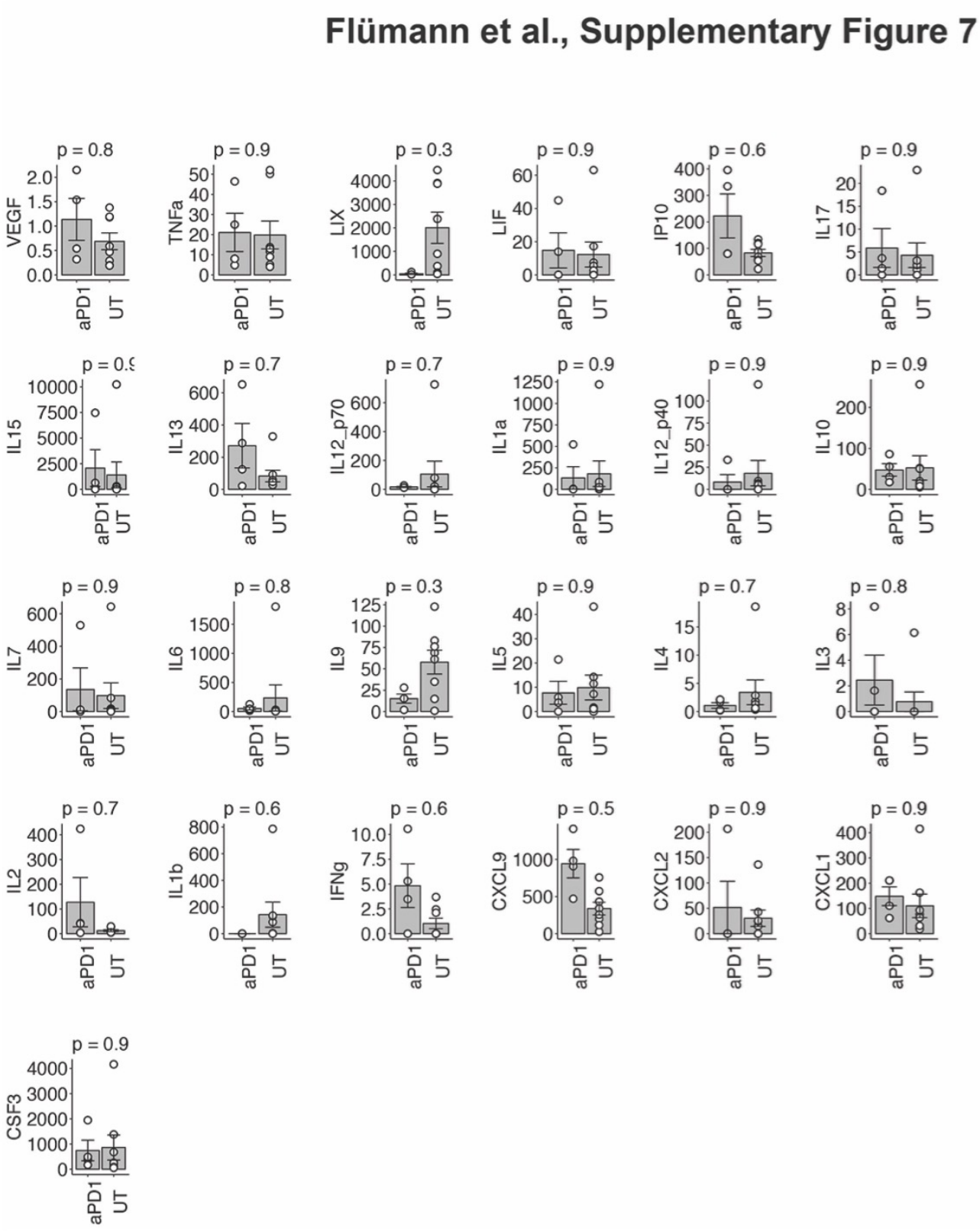


Supplementary Figure 5 – A) Cell lines were cultivated under continuous exposure to the IRAK4 inhibitors ND-2158 (5µM) and PF-06650833 (5µM) or the BTK inhibitor ibrutinib (5µM). Cells were

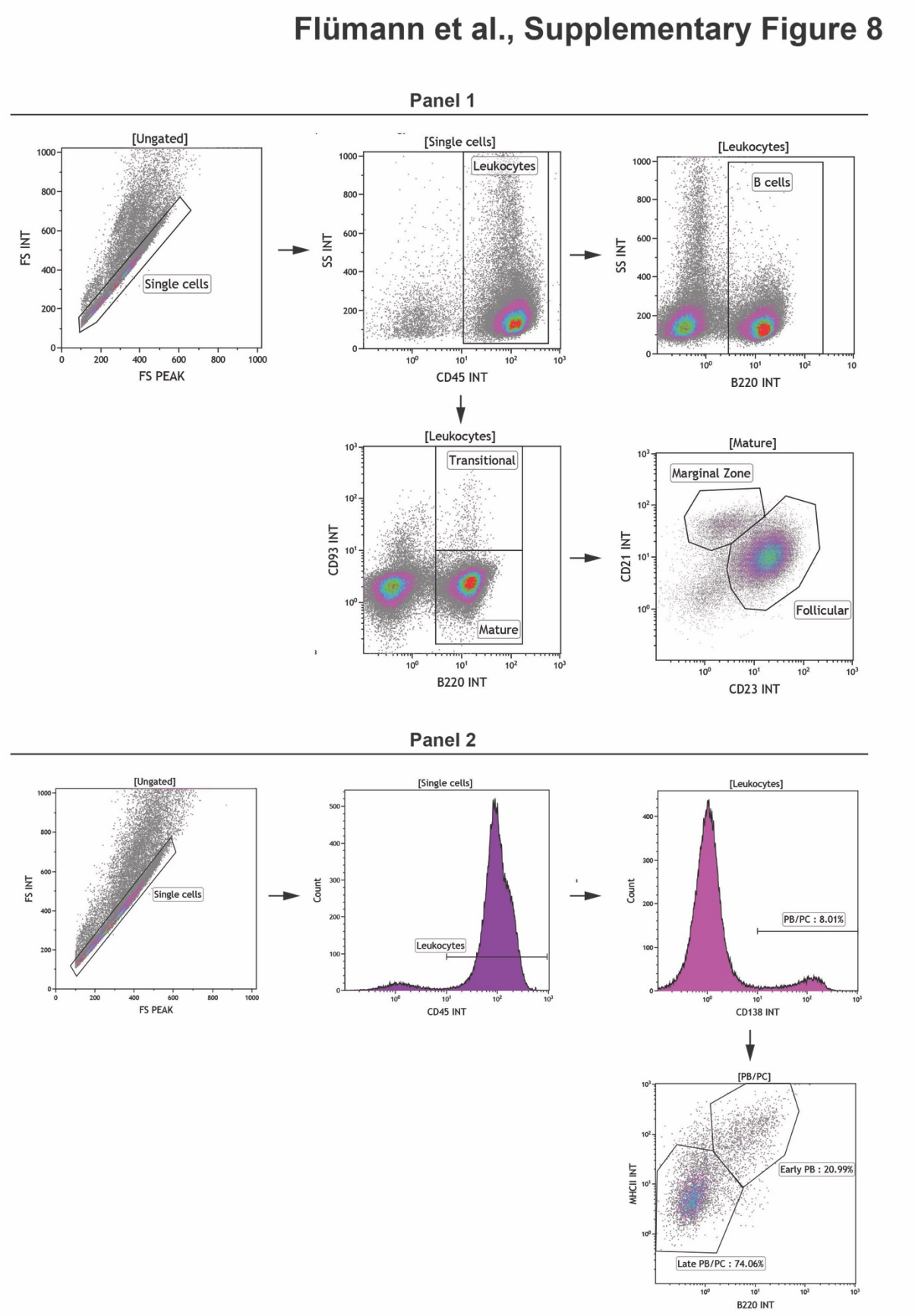
counted every third day and population doublings were calculated. **B)** Cell lines were screened for sensitivity against a panel of chemotherapeutics and small molecule inhibitors in a high-throughput manner. Cell viability was measured by CTG after 72 hours and the IC_{50} profiles were clustered in an unsupervised manner. IC50 values can be found in **Suppl. Table 2**.



Supplementary Figure 6 – A) A published RNA sequencing dataset (11) was analyzed for *BCL2* and *CD274* expression. ABC cases are illustrated in green, GCB cases in blue. The absolute case numbers of ABC and GCB cases and the frequency of ABC cases are given for each quartile. **B)** Illustrated are individual tumor volumes (normalized to baseline) over time. Crosses mark deaths.



Supplementary Figure 7 – Cytokine levels in the sera of 8 untreated and 4 α-PD-1 treated tumor-bearing animals were compared. Concentrations are given in pg/ml.



Supplementary Figure 8 – Illustration of the gating strategy used for the quantification of different B cell developmental stages in the spleen.