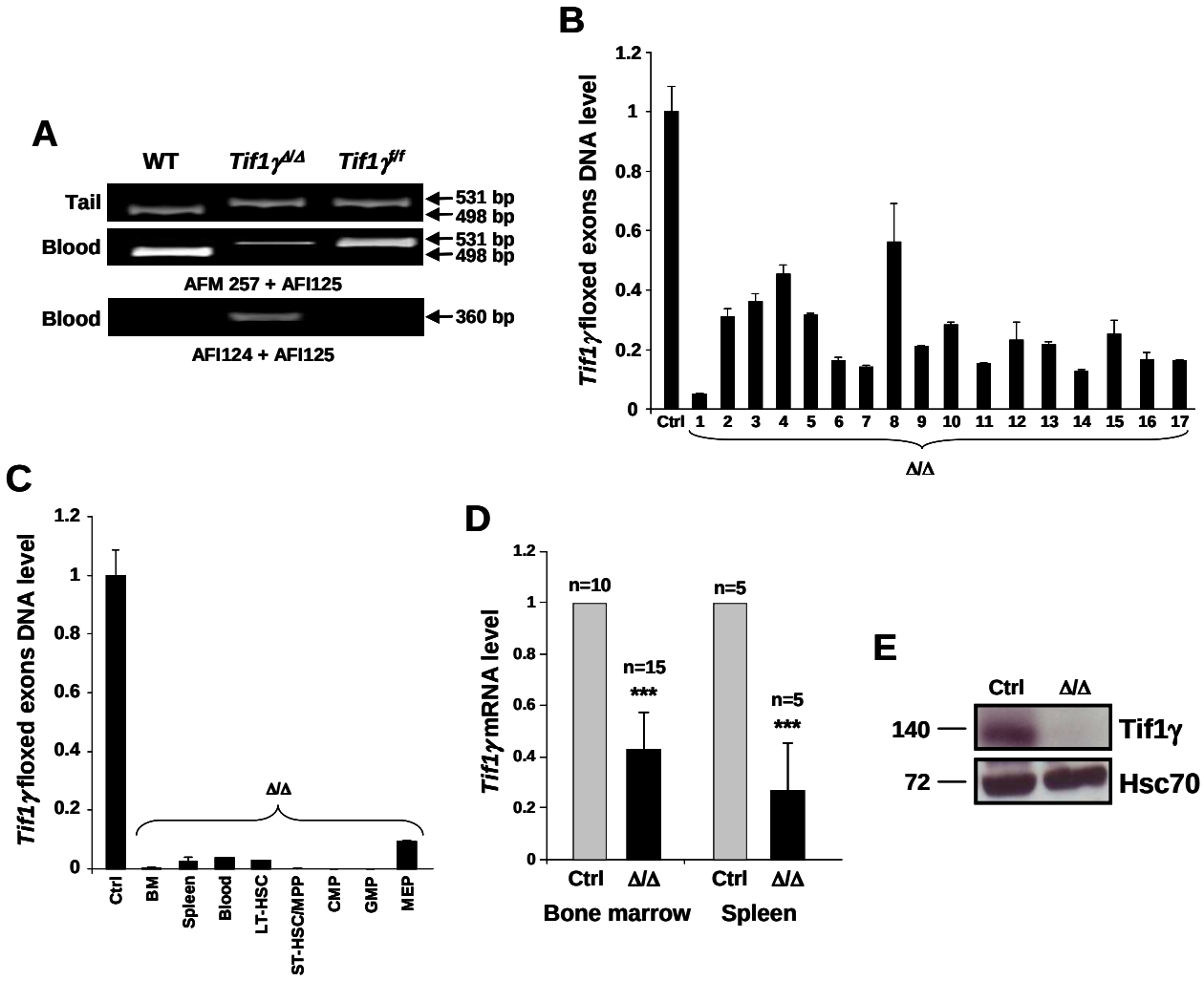
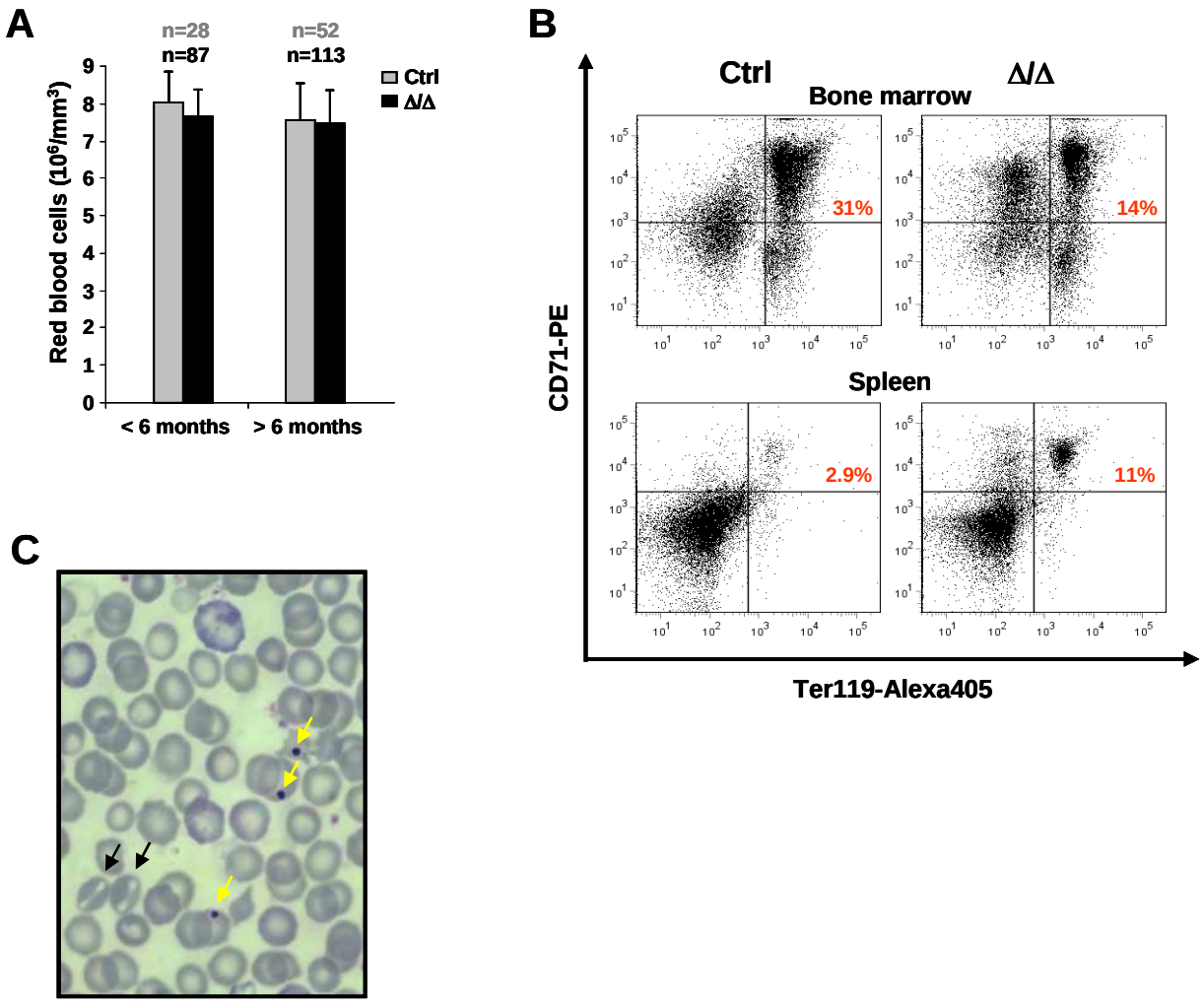
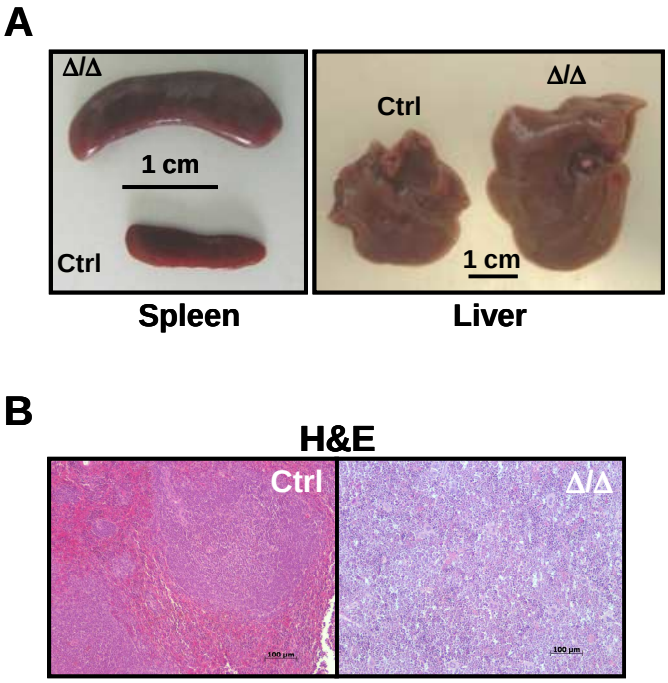


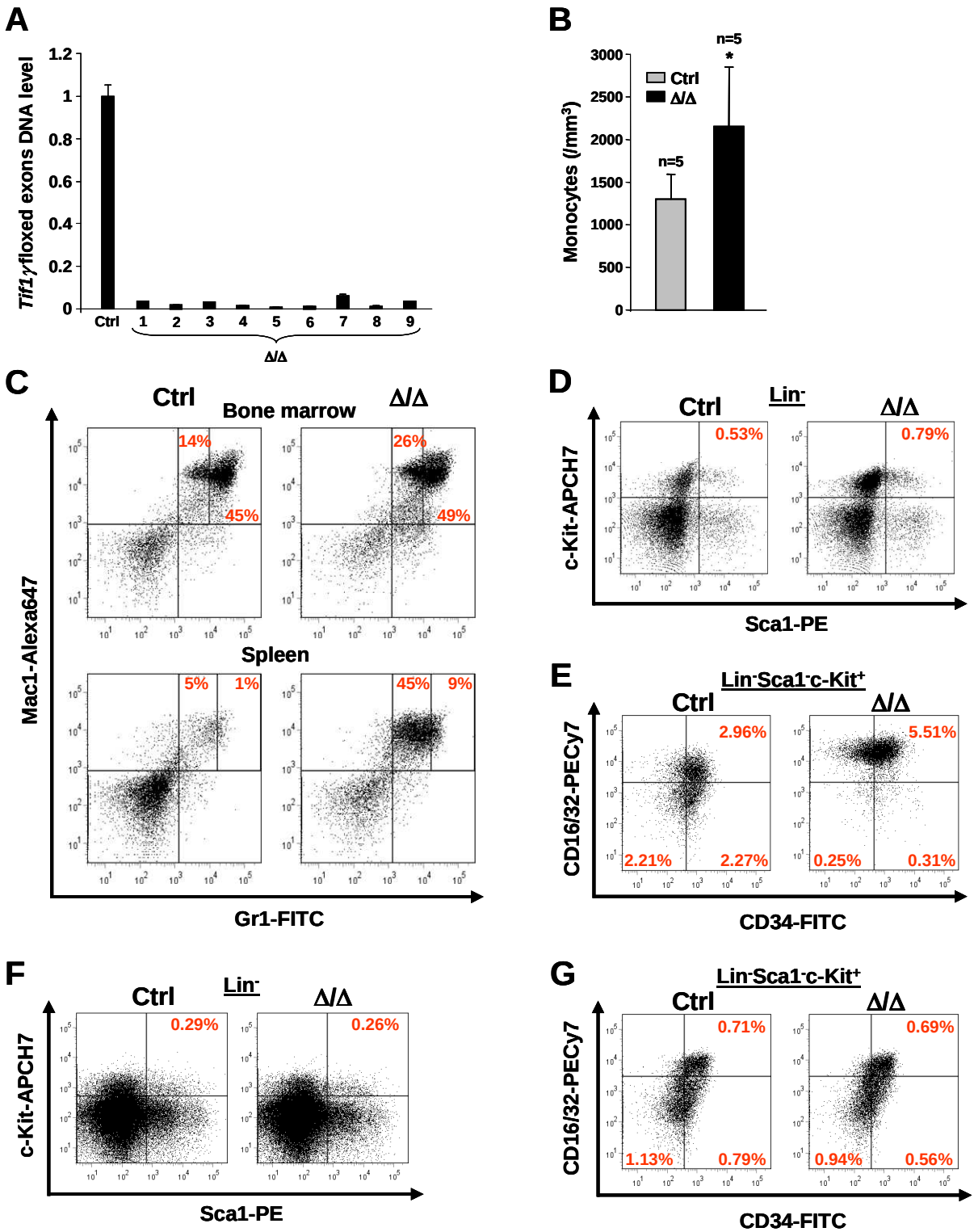
Supplemental figure 1. Genotyping and *Tif1γ* expression in *Tif1γ*$^{\Delta/\Delta}$ mice. (**A**) Representative PCR analysis of genomic DNA from tail or blood of wild type (WT), *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ), and *Tif1γ*$^{f/f}$ mice using a mixture of two primers. Amplification of the WT allele by forward and reverse primers AFM257 and AFI125 produces a 498 bp DNA fragment (lower band) while amplification of the floxed (*f*) allele results in a 531 bp DNA fragment (upper band), and amplification of the deleted (Δ) allele by forward and reverse primers AFI124 and AFI125 produces a 360 bp DNA fragment. (**B**) Q-PCR analysis of the *Tif1γ* floxed exons in peripheral blood cells from control (Ctrl) or *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice. Data are the means ± s.d. of the values from experiments performed in triplicate. (**C**) *Tif1γ* deletion, by Q-PCR analysis, in various hematopoietic tissues or cells. (**D**) RQ-PCR analysis of *Tif1γ* from total BM or spleen cells of control (Ctrl) or *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice. Data are the means ± s.d. of the values from independent experiments (**p* values are defined in Methods). (**E**) Tif1γ expression is decreased in *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice. Protein extracts were prepared from BM cells of control (Ctrl) or *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice then were electrophoresed on SDS-PAGE and immunoblotted with anti-Tif1γ antibody. Equivalent loading of lanes was controlled by the use of an anti-Hsc70 antibody.



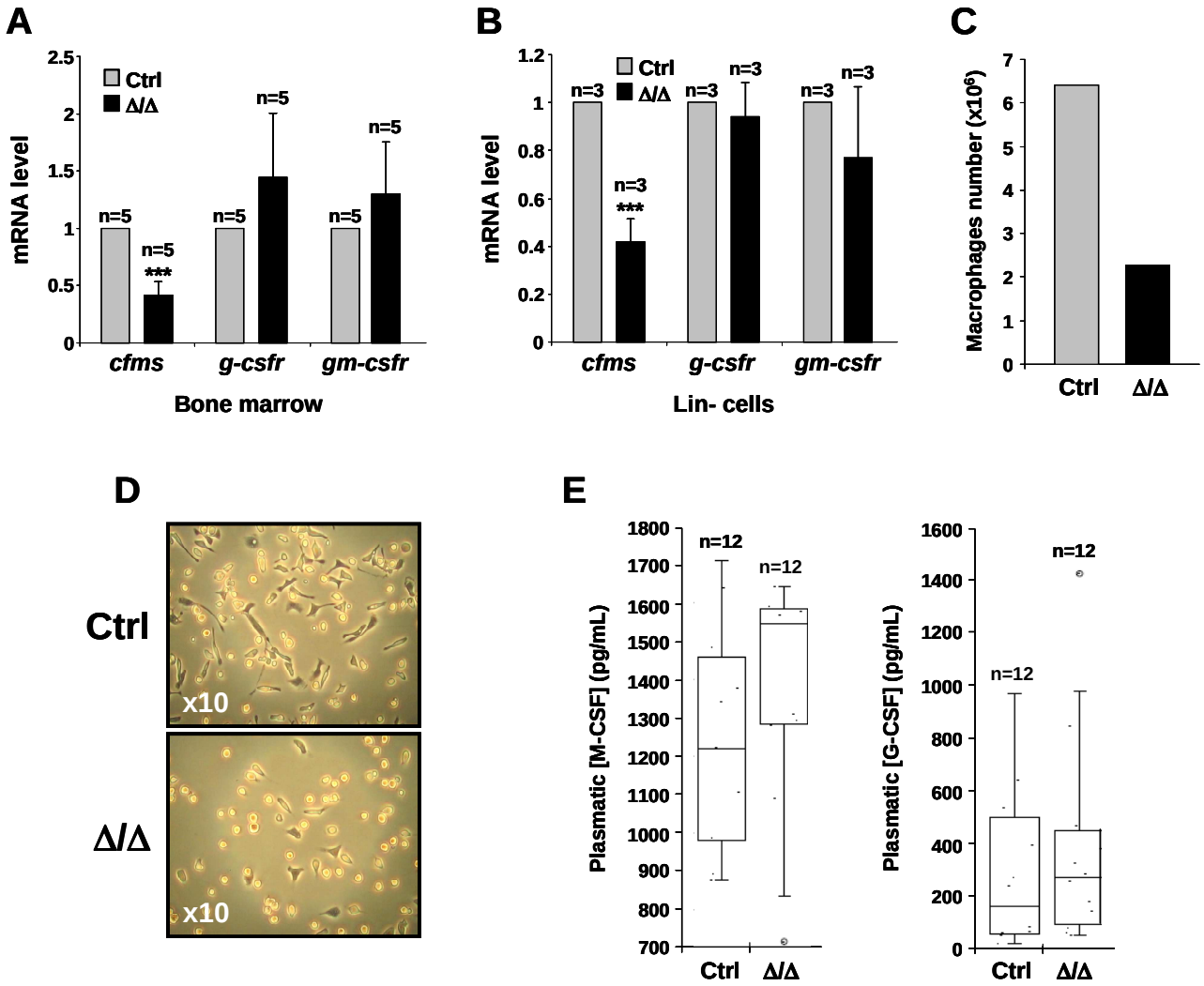
Supplemental figure 2. Erythroid defects in *Tif1γ*$^{\Delta/\Delta}$ mice. (**A**) Peripheral erythrocyte counts in control (Ctrl) and *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice, younger or older than 6 months. The results are shown as the means ± s.d. (**B**) FACS analysis of cell populations from BM and spleen of representative control (Ctrl) and *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice, older than 6 months demonstrated a decrease in BM associated with an increase in spleen of erythroblastic populations (Ter119^{+}CD71^{+}) in *Tif1γ*$^{\Delta/\Delta}$ mice. (**C**) Representative MGG stained peripheral blood smears (×100) from *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice, older than 6 months, demonstrated the presence of Howell-Joly bodies (yellow arrows) and stomatocytes (black arrows).



Supplemental figure 3. Hepatosplenomegaly in *Tif1γ*$^{\Delta/\Delta}$ mice. (**A**) Marked splenomegaly (left panel) in a *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mouse (top) as compared with the spleen of a wild-type sex and age-matched control (Ctrl) mouse (bottom). Marked hepatomegaly (right panel) in a *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mouse (right) as compared with the liver of a wild-type sex and age-matched control (Ctrl) mouse (left). (**B**) H&E staining of paraffin-embedded spleen sections from representative control (Ctrl) or *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice demonstrated the infiltration of hematopoietic populations in *Tif1γ*$^{\Delta/\Delta}$ mice.



Supplemental figure 4. Mice transplanted with *Tif1γ*$^{Δ/Δ}$ bone marrow develop a myeloproliferative disease. (**A**) Q-PCR analysis of the *Tif1γ* floxed exons in PB from control (Ctrl) or *Tif1γ*$^{Δ/Δ}$ (Δ/Δ) transplanted mice. Data are the means ± s.d. of the values from experiments performed in triplicate. (**B**) Peripheral monocyte counts in Ctrl or Δ/Δ transplanted mice. The results are shown as the means ± s.d. (**C**) (Upper panel) Flow cytometry analysis of cell populations from total BM cells of mice transplanted with BM from representative Ctrl or Δ/Δ mice. (Lower panel) Flow cytometry analysis of cell populations from spleen of mice transplanted with BM from representative Ctrl or Δ/Δ mice. (**D**) Flow cytometry analysis of cell populations from total BM cells of mice transplanted with BM from representative Ctrl or Δ/Δ mice. (**E**) Representative FACS staining profiles of the progenitor populations, including CMPs (lower right panel), MEPs (lower left panel), and GMPs (upper right panel), from the respective Ctrl or Δ/Δ transplanted mice. (**F** and **G**) *Tif1γ*$^{Δ/Δ}$ mice transplanted with control BM cells do not develop a myeloproliferative disease. Control BM cells were transplanted into lethally irradiated Δ/Δ or Ctrl recipient mice. Differences observed in the distribution of LSK cells and progenitors of control mice between panels D, E and F, G may be explained by the genetic background of the recipient mice. Flow cytometry analysis of cell populations from total BM of representative control Ctrl or Δ/Δ mice.



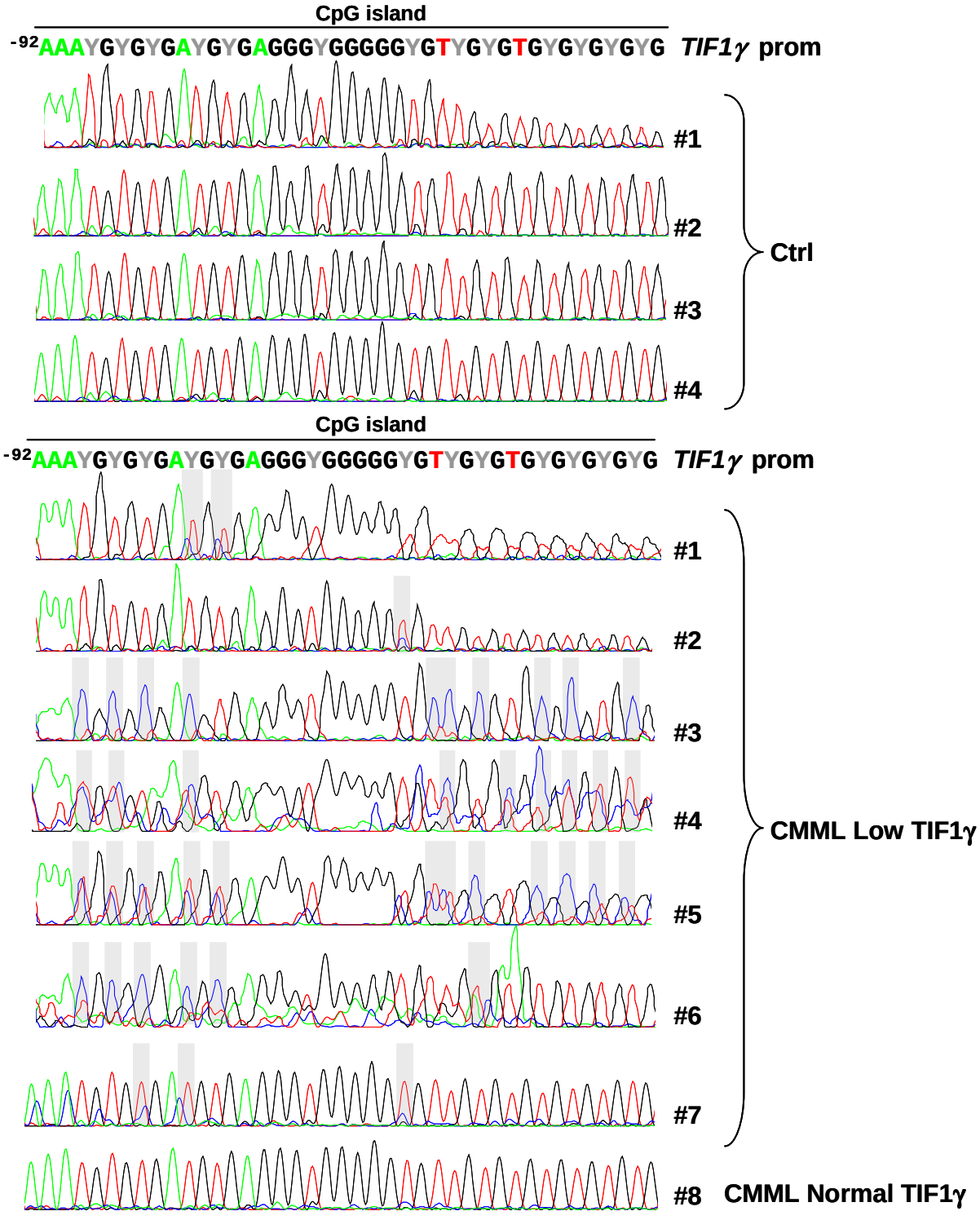
Supplemental figure 5. Tif1γ deficiency decreases *cfms* expression and alterates macrophage differentiation. (**A**) (**B**) RQ-PCR analysis of *cfms*, *g-csfr*, *and gm-csfr* from total BM (left panel) or Lin- cells (right panel) of control (Ctrl) or *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice. Data are the means ± s.d. of the values from independent experiments (**p* values are defined in Methods). (**C**) ***Tif1γ*** deletion results in decreased macrophages in the peritoneum. The total number of intraperitoneal macrophages from control (Ctrl) and *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice is summarized. (**D**) Photomicrographs of control (Ctrl) or *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) peritoneal macrophages cultured during 24h. (**E**) Plasmatic concentration of M-CSF and G-CSF from control (Ctrl) and *Tif1γ*$^{\Delta/\Delta}$ (Δ/Δ) mice.

	Low Tif1γ	Normal Tif1γ
Number of cases	21	39
Mean age [range]	73.2 [51-91]	72.1 [50-84]
Sex ratio	2	2.1
At diagnosis		
Mean hemoglobin g/L [range]	119 [71-149]	117 [84-140]
Mean platelet count 10^9/L [range]	155 [10-300]	137 [3-379]
Mean leucocyte count 10^9/L [range]	19.0 [3.8-92.7]	14.4 [2.0-85.6]
Mean monocyte count 10^9/L [range]	5.1 [1-46]	4.4 [1-30.8]
>13.10^9 monocyte/L (%)	53%	32%

Supplemental table 1. Clinical and biological characteristics of the CMML patients in whom *Tif1γ* mRNA expression was analyzed.

	All
Number of cases	66
Mean age [range]	70.37 [50-93]
Sex ratio	2.14
At diagnosis	
Mean hemoglobin g/L [range]	116 [52-163]
Mean platelet count 10^9/L [range]	163 [3-411]
Mean leucocyte count 10^9/L [range]	14.3 [3.5-85.6]
Mean monocyte count 10^9/L [range]	3.3 [1-30.8]
>13.10^9 monocyte/L (%)	46%

Supplemental table 2. Clinical and biological characteristics of the CMML cohort used for *TIF1γ* sequencing.



Supplemental figure 6. *TIF1γ* is an epigenetically-regulated tumor suppressor gene in CMML. Sequencing of the bisulfite modified *TIF1γ* promoter sequence from normal monocytes of healthy donors (Ctrl) or CMML patients. CMML patient #8 is a representative patient who harbors a normal level of TIF1γ.