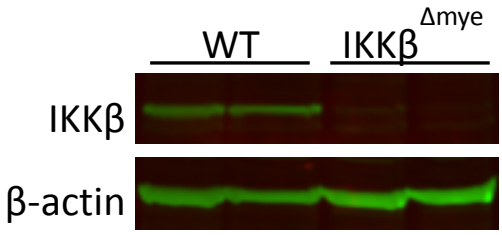

Figure S1 (Related to Figure 1).

Expression of IKKβ protein by western blot in bone marrow cells from WT and IKKβ$^{\Delta mye}$ mice showing deletion of IKKβ in IKKβ$^{\Delta mye}$ mice.

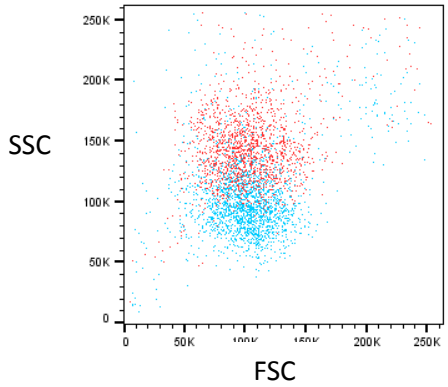

Figure S2 (Related to Figure 2).

FACS plot showing forward scatter (FSC) and side scatter (SSC) of $CD11b^{+}/Gr1^{hi}$ (red) and $CD11b^{+}/Gr1^{low/neg}$ (blue) cells. $CD11b^{+}/Gr1^{hi}$ cells have higher SSC, indicating increased intracellular complexity, which is characteristic of neutrophils.

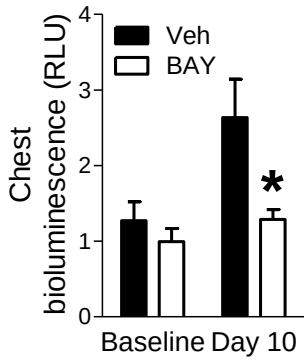

Figure S3 (Related to Figure 6).

BAY 11-7082 treatment blocks NF-κB activation in reporter mice. NF-κB reporter mice were injected with a single dose of urethane and treated with BAY 11-7082 (10 mg/kg by IP injection) or vehicle control 3 times per week. Chest bioluminescence was measured at baseline (prior to urethane treatment) and 10 days after urethane injection (RLU = relative light units). NF-κB reporter mice that express a green fluorescent protein-luciferase fusion protein under control of an NF-κB dependent promoter were injected intravenously with D- luciferin (1 mg) followed by bioluminescent imaging.

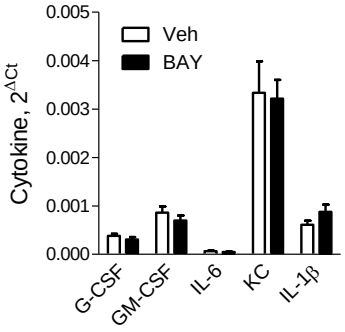

Figure S4 (Related to Figure 6).

Expression of cytokines by mRNA in the lungs of WT mice injected with urethane and treated with BAY 11-7082 (10 mg/kg) or vehicle control (Veh) for 1 week.

Table S1 (Related to Figure 6).

Characteristics of NSCLC patients treated with bortezomib.

Patient Characteristics	**Total (n=28)**
Age, y	75.5 (68.5, 79.2)*
Male gender	22 (78.6%)†
Cancer stage	
IIIB	1 (3.6%)†
IV	27 (96.4%)†
Cancer histology	
Adenocarcinoma	11 (39.3%)†
Squamous	11 (39.3%)†
Other NSCLC	6 (21.4%)†
Performance score	
0	19 (67.9%)†
1	9 (32.1%)†
Progression-free survival, mo	3.6 (1.7, 6.4)*
Overall survival, mo	10.2 (4.7, 21.0)*

*Data are represented as median (interquartile range)

†Data are represented as total (percent)

Supplemental Experimental Procedures

Bronchoalveolar lavage (BAL)

BAL cells were collected and counted as previously described (Stathopoulos et al., 2007).

Histology and immunohistochemistry.
Lung tumors and atypical adenomatous hyperplasia (AAH) lesions were counted as previously described (Zaynagetdinov et al., 2011). For proliferation and apoptosis analyses, lung sections were immunostained with antibodies against PCNA (Life Technologies) or cleaved caspase-3 (Cell Signaling). Proliferation and apoptosis indices were calculated by counting the number of positive cells per 40x field and averaged from 25 randomly chosen fields.

Isolation of lung cells and flow cytometry/FACS
Lung single-cell suspensions were prepared as described (Zaynagetdinov et al., 2011). Cells were stained with the following antibodies: CD45 - APC-Cy7, CD11b - V450, Gr1 - PerCP-Cy5.5 (BioLegend); Ly6C - FITC and Ly6G - PerCP-Cy5.5 (BD Bioscience); MPO – FITC (Abcam). Flow cytometry was performed using the BD LSR II flow cytometer (BD Bioscience). Data were analyzed with FlowJo software (TreeStar). $CD11b^+$ cells were purified by magnetic separation using microbeads (Miltenyi Biotec) followed by FACS based on expression of Ly6G and Ly6C.

Western blot
Whole lung lysates were prepared using CelLytic^{TM} MT Cell Lysis Reagent (C3228; Sigma-Aldrich), separated by SDS-PAGE gel, transferred to nitrocellulose membrane, and probed with the anti-IKKβ (10AG2; Novus Biologicals) and anti-β-actin (A5316; Sigma-Aldrich). Immunodetection was performed using the corresponding AlexaFluor-conjugated antibodies and the Odyssey Infrared Imaging System (LI-COR Biosciences).

Allogenic mixed leukocyte reaction (MLR) assay
Responder $CD4^+/CD25^-$ effector T cells (Teff) from spleens of naive FVB mice ($1x10^5$ per well) were labeled with CFSE (5 mM; Life Technologies) and activated with allogeneic mature bone marrow-derived dendritic cells from C57BL/6 mice. The suppressive function of $CD11b^+/Ly6G^+$ lung neutrophils from $IKK\beta^{\Delta mye}$ mice was tested on the proliferation of CFSE-labeled Teff cells by flow cytometry. Dead cells were excluded from analysis on the basis of staining with DAPI (4-6-Diamidino-2-phenylindole, Life Technologies).

Protein expression
G-CSF, GM-CSF, IFNγ, IL-4, IL-6, IL-10, IL-12p40, KC, MCP-1, and MIP-1α concentrations were measured by the MILLIPLEX MAP Mouse Cytokine/Chemokine Panel (Millipore). Murine IL-1β protein was measured by ELISA (BioLegend). Human plasma IL-1β, IL-6, IL-8, and TNF were measured using the BD^{TM} Cytometric Bead Array Human Enhanced Sensitivity Flex Sets (BD Biosciences).

***In vitro* inhibitor studies**
Equal numbers of cells (0.15×10^6) were seeded into 96-well plates. Cells were cultured for 1 hour in the presence of Ac-YVAD-CMK (100μM; N-1330.0005; Bachem), MeOSuc-APPV-CMK (100μM; CAS 65144-34-5; Santa Cruz Biotechnology), or Z-GLP-CMK (100μM; 03CK00805; MP Biomedicals).

Bone marrow transplantation
Lethally irradiated (9.5 Gy) recipient mice were injected with bone marrow cells (2×10^6 bone marrow cells/mouse in PBS) from sex-matched, syngeneic donor mice. Animals were then housed for eight weeks under specific pathogen free (SPF) conditions with access to acidified water (pH 2.0) containing neomycin (100 mg/L, Sigma-Aldrich) and polymyxin B (10 mg/L, Sigma-Aldrich) from 3 days before transplantation until 14 days after transplantation. Mice were used for studies 8 weeks following transplantation.

Real-time PCR
RNA from lung tissue or sorted myeloid cells was isolated using the RNeasy Mini kit (Qiagen). cDNA was generated using SuperScript III Reverse Transcriptase (Life Technologies) and subjected to Real-Time PCR using SYBR Green PCR Master Mix (Life Technologies). PCR primers are listed below. Relative mRNA expression in each sample was normalized to GAPDH and presented using the comparative Ct method ($2^{\Delta Ct}$).

Table S2. (Related to Figures 4 and 5).

Primer sets used in this study.

Gene	Forward Primer (5'→3')	Reverse Primer (5'→3')
G-CSF	TTGGTGAGTGGGGTTGCCATAGGT	TGCCCTCTTCTCATTTGTGCTCCT
GM-CSF	CGTTGGTGAGTGAGGGAGAGAGTT	TGAAAGGCAGGGCAAGACAAGG
IL-6	AAAGAGTTGTGCAATGGCAATTCT	AAGTGCATCATCGTTGTTCATACA
KC	CCGAAGTCATAGCCACACTCAA	GCAGTCTGTCTTCTTTCTCCGTTAC
IL-1β	GCAACTGTTCCTGAACTCAACT	ATCTTTTGGGGTCCGTCAACT
CatG	GCCAATCGCTTCCAGTTCTAC	GTGGGTGTTCACATTCTTACCC
TNFα	AAGCCTGTAGCCCACGTCGTA	GGCACCACTAGTTGGTTGTCTTTG
IL-12p35	TGGACCTGCCAGGTGTCTTAG	CAATGTGCTGGTTTGGTCCC
ICAM1	TGCCTCTGAAGCTCGGATATAC	TCTGTCGAACTCCTCAGTCAC
IFNγ	GCGTCATTGAATCACACCTGA	CTCGGATGAGCTCATTGAATGC
iNOS	CACCTTGGAGTTCACCCAGT	ACCACTCGTACTTGGGATGC
CCL2	TTAAAAACCTGGATCGGAACCAA	GCATTAGCTTCAGATTTACGGGT
CCL5	ACCATGAAGATCTCTGCAGC	TGAACCCACTTCTTCTCTGG
CCL17	TGCTTCTGGGGACTTTTCTG	CATCCCTGGAACACTCCACT
VEGF	TTACTGCTGTACCTCCACC	ACAGGACGGCTTGAAGATG
IL-10	ACCTGCTCCACTGCCTTGCT	GGTTGCCAAGCCTTATCGGA
Arg1	GATTGGCAAGGTGATGGAAG	TCAGTCCCTGGCTTATGGTT
GAPDH	TGAGGACCAGGTTGTCTCCT	CCCTGTTGCTGTAGCCGTAT