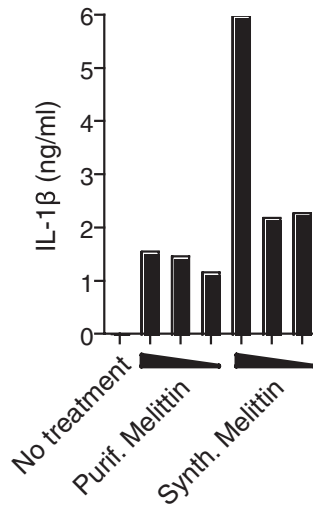
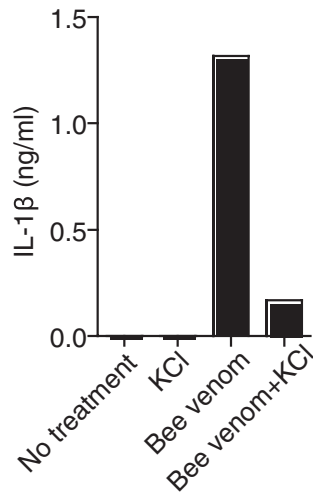


# Supporting Information

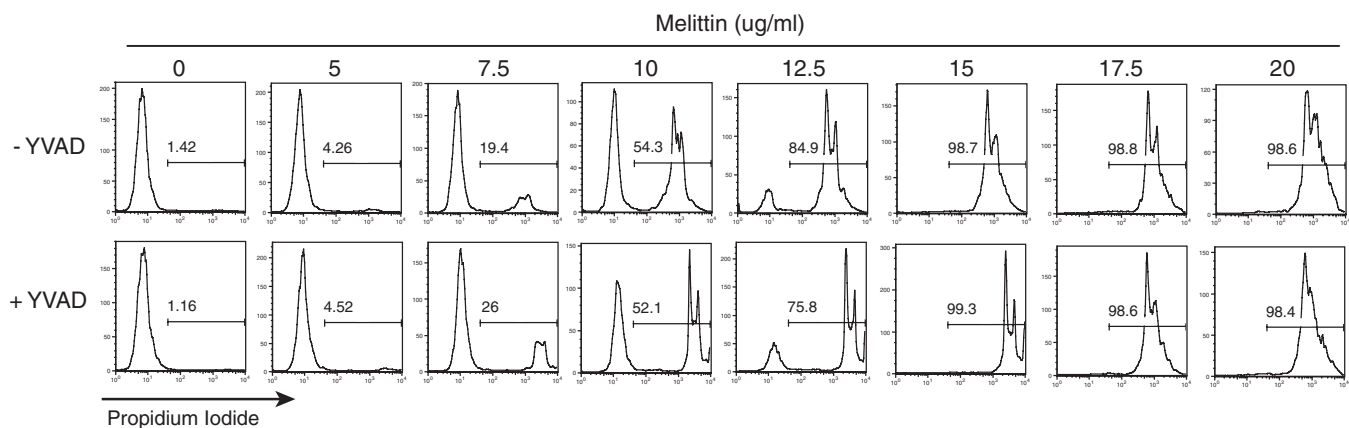
Palm and Medzhitov 10.1073/pnas.1221476110



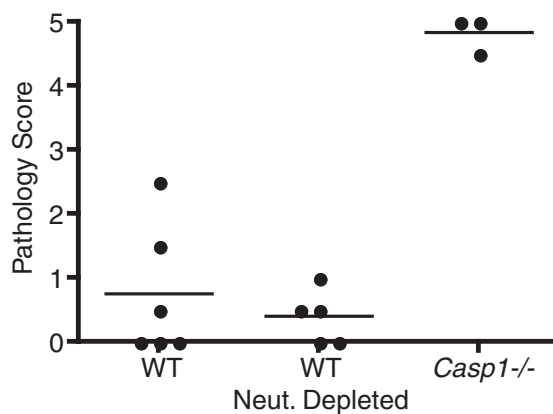
**Fig. S1.** Synthetic melittin induces IL-1 $\beta$  secretion by LPS-treated macrophages. Bone-marrow-derived macrophages were treated with LPS for 4 h before stimulation with melittin purified from bee venom (3.1, 1.56, 0.78  $\mu$ g/mL) or synthetically produced melittin (3.1, 1.56, 0.78  $\mu$ g/mL) for 1 h. IL-1 $\beta$  secretion was measured by ELISA.



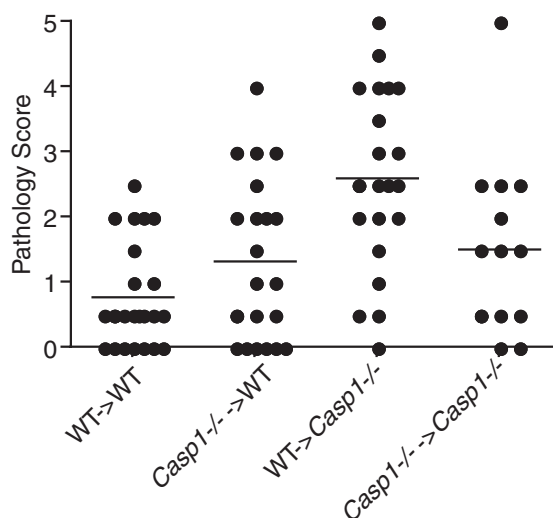
**Fig. S2.** High extracellular potassium blocks bee-venom-induced IL-1 $\beta$  secretion. Bone-marrow-derived macrophages incubated with or without additional KCl (50 mM) were treated with LPS for 4 h before stimulation with bee venom (12.5  $\mu$ g/mL) for 1 h. IL-1 $\beta$  secretion was measured by ELISA.



**Fig. S3.** Caspase-1 does not protect against melittin-induced cell death in Chinese hamster ovary cells. Chinese hamster ovary cells that were or were not pretreated for 1 h with the caspase-1 inhibitor Z-Tyr-Val-Ala-Asp(OMe)-fluoromethylketone (100 µM) were treated with titrating doses of melittin. Cell death was measured by propidium iodide staining of cells 3 h after melittin treatment.



**Fig. S4.** Neutrophil depletion does not affect formation of necrotic lesions after s.c. injection with Western Diamondback venom. WT mice, neutrophil-depleted mice, and *Casp1*<sup>-/-</sup> mice were injected s.c. with Western Diamondback venom (65 µg) and necrotic lesions were scored on day 5 after injection. Mice were depleted of neutrophils using the depleting antibody RB6-8C5 (0.2 mg intraperitoneally every 24 h starting 1 d before injection with venom).



**Fig. S5.** Caspase-1 in nonhematopoietic cells enhances resistance to s.c. injection with Western Diamondback venom. Radiation bone marrow chimeras between WT and *Casp1*<sup>-/-</sup> mice (donor→recipient) were constructed by i.v. injection of 10 million donor bone marrow cells into irradiated recipients (900 rads). After 8 wk of reconstitution, mice were injected s.c. with Western Diamondback venom (65 µg) and necrotic lesions were scored on day 5 after injection.