Figure S1. **cGAMP induces K⁺/Ca²⁺- and ROS-dependent inflammasomes.** (a and b) IL-1β ELISAs from supernatants of BMDMs primed with LPS and treated with vehicle or 2-APB (a) or N-acetyl-cysteine (NAC; b) at the indicated concentrations followed by transfection with 2′3′-cGAMP for 6 h. (c) IL-1β ELISAs from BMDMs primed with LPS, followed by transfection with 2′3′-cGAMP. Extracellular KCl added for the last 1, 2, or 3 h of induction. n = 3 independent experiments. Error bars, SD; ****, P < 0.0001.
Figure S2. **cGAMP induces complexes containing both NLRP3 and AIM2.** Confocal microscopy of JAWSII cells expressing AIM2-Flag pulsed with doxycycline during LPS priming. (a–c) Cells were transfected with 2′3′-cGAMP (a), a 30:1 mixture of 2′3′-cGAMP and fluorescein-labeled 2′3′-cGAMP (b), or rhodamine-dAdT followed by FLICA-660 (c). Cells were labeled with primary antibodies to Asc, Nlrp3, and Flag (for AIM2-Flag) followed by Alexa Fluor-labeled secondary antibodies. Shown are pseudocolored images. Bars, 5 µm.

Figure S3. **Bronchiolar macrophage cell count after cGAMP administration.** WT, Aim2−/−, Nlrp3−/−, and Aim2−/− Nlrp3−/− DKO mice were intranasally dosed with 2′3′-cGAMP followed by a second dose 24 h later. 4 h after the second dose, BALF was collected, and cells were cytopun onto slides and stained with Diff-Quick solution for cell differentiation. Shown are total counts of bronchial macrophages. WT, n = 17; Aim2−/−, n = 10; Nlrp3−/−, n = 8; Aim2−/− Nlrp3−/− DKO, n = 8. Results are presented as the mean ± SEM.