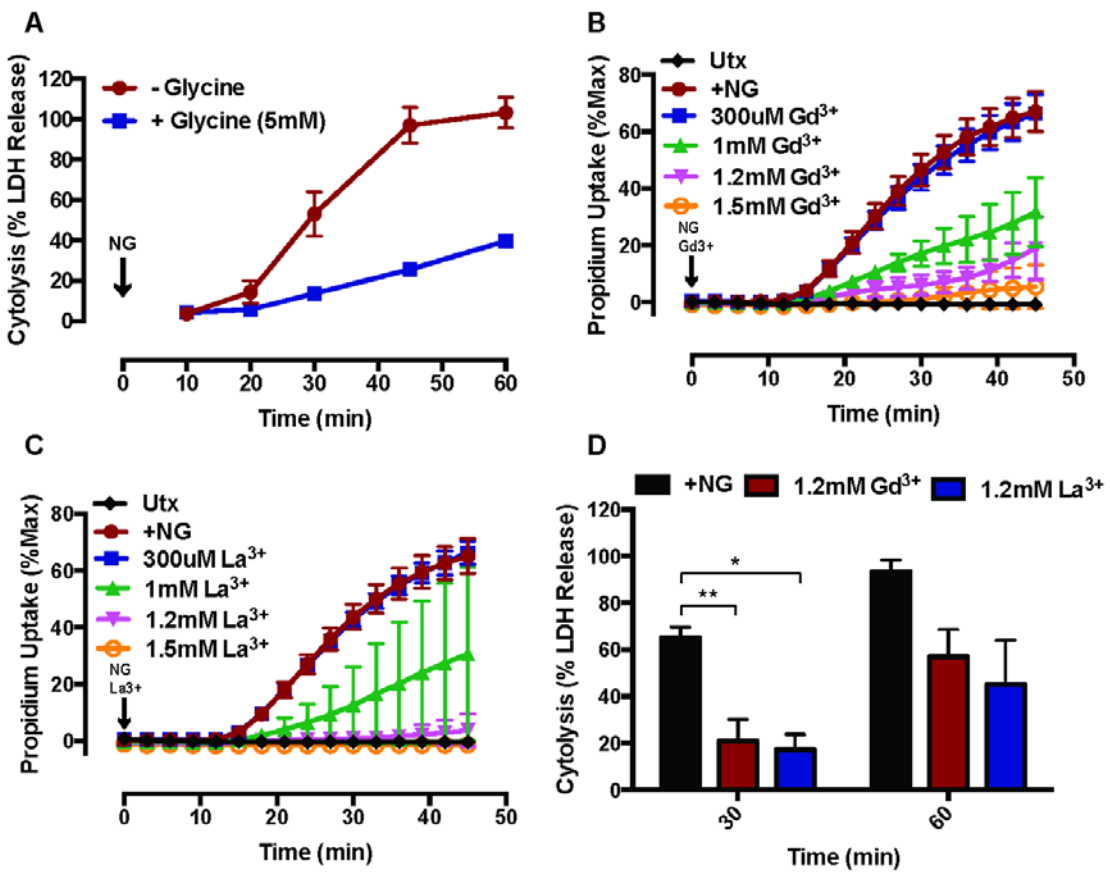
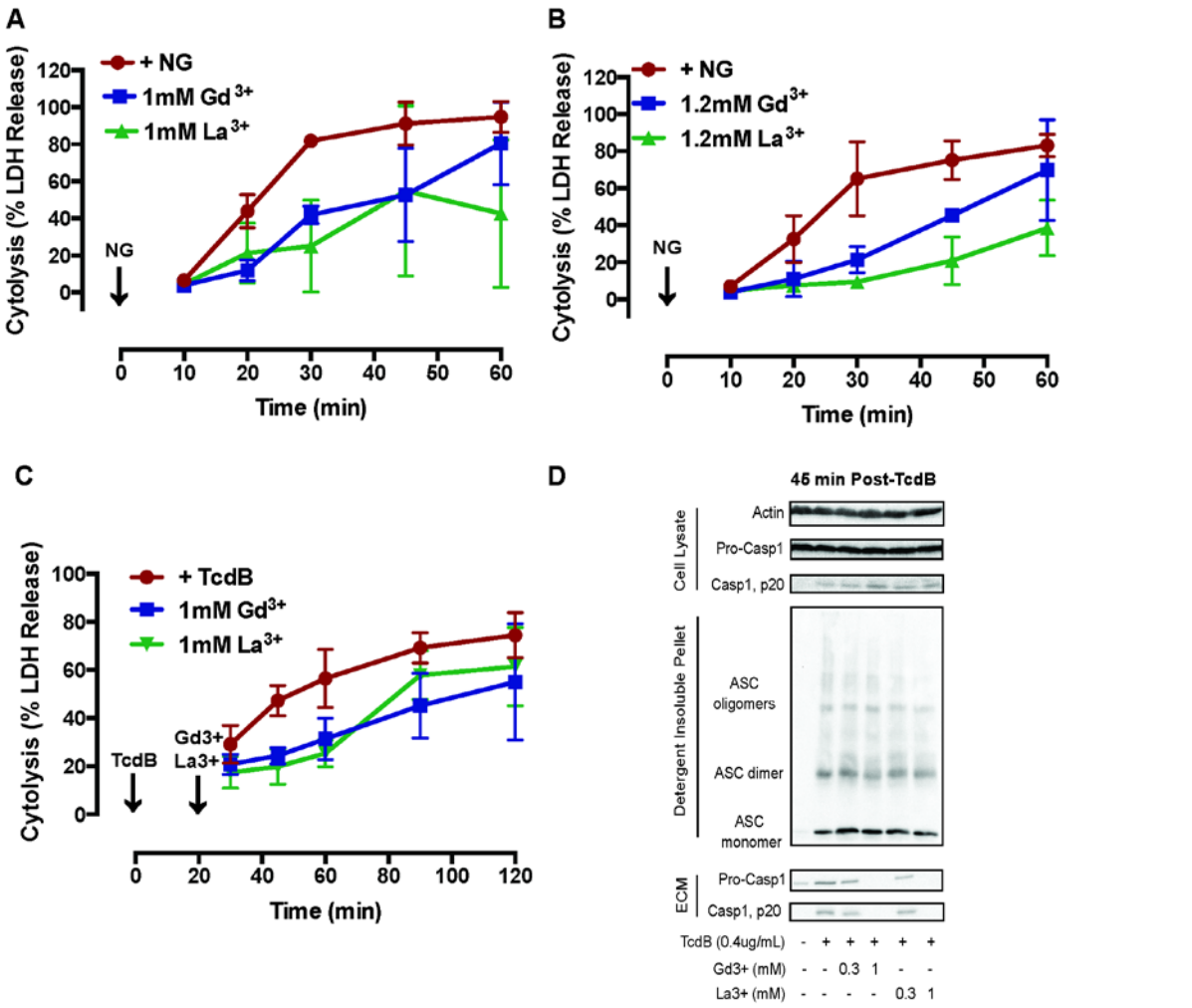
Supplemental Figure 1



Supplemental Figure 1. *Lanthanides coordinately suppress both the Gsdmd-dependent plasma membrane permeability change and pyroptotic lysis induced by NLRP3 inflammasome activation in iBMDM*

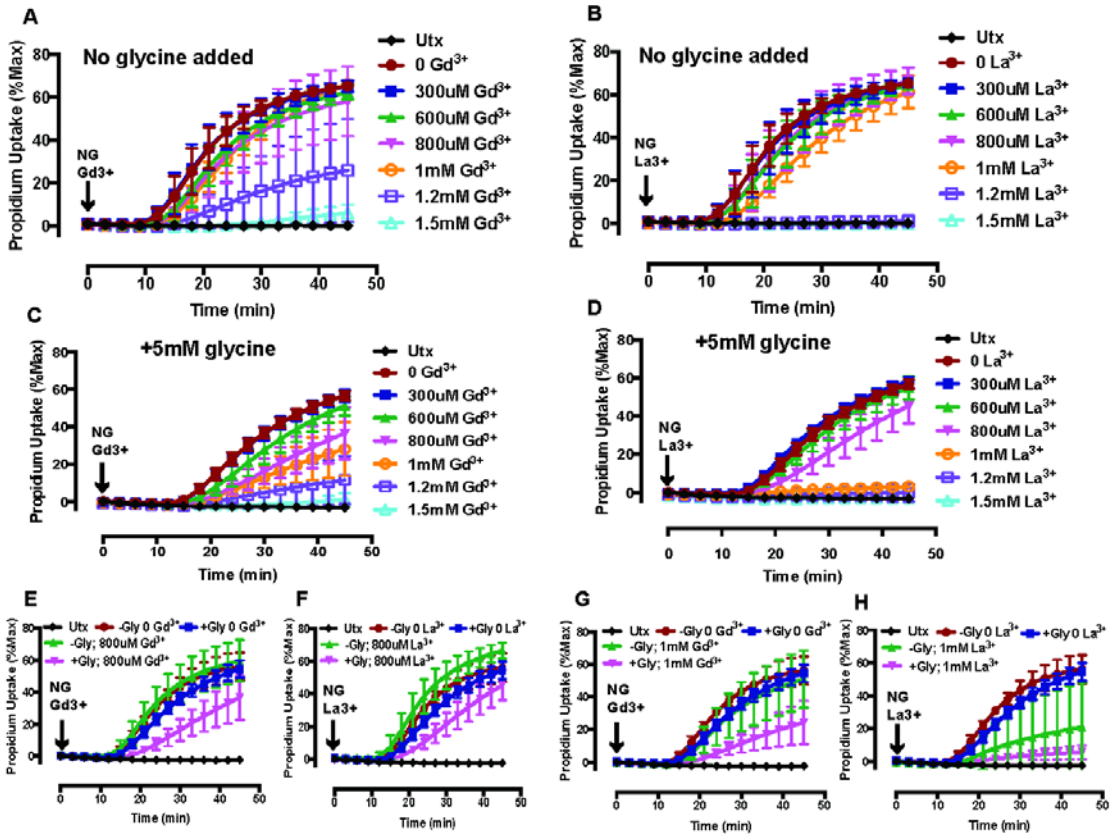
(A) LPS-primed WT iBMDM were stimulated with NG (10μM) in the presence or absence of glycine (5mM). At the indicated times, supernatants were assayed for LDH activity as described in Fig. 1. These data represent the mean ± SE of 4 replicates from 2 independent experiments. **(B)** LPS-primed WT iBMDM were stimulated with NG in the presence or absence of Gd^{3+} (0.3, 1, 1.2, 1.5mM) or **(C)** La^{3+} (0.3, 1, 1.2, 1.5mM) for 45 min, and propidium^{2+} fluorescence was quantified every 3 min as described in Fig. 1. These data represent the mean ± SE of 4 replicates from 2 independent experiments. **(D)** LPS-primed WT iBMDM were stimulated with NG for 30 or 60 min in the presence or absence of 1.2mM Gd^{3+} or La^{3+}, and the supernatants were subsequently assayed for LDH activity. These data represent the mean ± SE of 4 replicates from 2 independent experiments.

Supplemental Figure 2



Supplemental Figure 2. *Lanthanides delay the execution of pyroptotic cell death following NLRP3 or Pyrin inflammasome activation and do not inhibit pyrin inflammasome activation* **(A)** LPS-primed WT BMDM were stimulated with NG (10μM) in the presence or absence of 1mM Gd^{3+} or La^{3+} or **(B)** 1.2mM Gd^{3+} or La^{3+}. At the indicated times, supernatants were assayed for LDH activity as described in Fig. 1. These data represent the mean ± SE of 4 replicates from 2 independent experiments. **(C)** LPS-primed WT BMDM were stimulated with TcdB (0.4μg/mL) in the presence or absence of 1mM Gd^{3+} or La^{3+}. Gd^{3+} and La^{3+} were added 20 min after TcdB. At the indicated times, supernatants were assayed for LDH activity. These data represent the mean ± SE of 4 replicates from 2 independent experiments. **(D)** LPS-primed WT BMDM were stimulated with TcdB (0.4μg/mL) for 45 min in the presence or absence of Gd^{3+} or La^{3+} (0.3mM and 1mM). Gd^{3+} and La^{3+} were added 20 min after TcdB. The ECM and soluble lysate were analyzed on western blot for the presence of caspase-1. The soluble lysate was also probed for actin. The detergent insoluble fraction was DSS crosslinked and analyzed on western blot for the presence of oligomerized ASC. These data are representative of results from 3 experiments.

Supplemental Figure 3



Supplemental Figure 3. *Lanthanides exhibit more potent suppression of pyroptotic propidium influx in the presence of glycine in a dose-dependent manner*
(A,C) LPS-primed WT BMDM were stimulated with NG (10μM) for 45 min in the presence of increasing Gd^{3+} and **(B,D)** La^{3+} concentrations in the **(A,B)** absence or **(C,D)** presence of 5mM glycine. $Propidium^{2+}$ fluorescence was quantified every 3 min as described in Fig. 1. These data represent the mean ± SE of 4-8 replicates from 2-4 independent experiments. **(E)** LPS-primed WT BMDM were stimulated with NG (10μM) in the presence or absence of 5mM glycine and with or without 800μM Gd^{3+} or **(F)** La^{3+} for 45 min, and $propidium^{2+}$ fluorescence was quantified every 3 min. **(G)** WT BMDM were stimulated as in (E) in the presence or absence of 1mM Gd^{3+} or **(H)** La^{3+}, and $propidium^{2+}$ fluorescence was quantified every 3 min. These data represent the mean ± SE of 4-6 replicates from 2-3 independent experiments.

Supplemental Table 1. *Physical properties of lanthanides and various DNA-intercalating cationic dyes*

DNA-Intercalating Dye or Lanthanide	Compound Formula	Compound Mol Mass	Free Cation	Free Cation Mol Mass
Ethidium Bromide	Eth(Br)	394.24	Eth^{+}	314.39
YoPro Iodide	$YoPro(I)_2$	629.32	$YoPro^{2+}$	375.52
Propidium Iodide	$Pro(I)_2$	668.40	$Propidium^{2+}$	414.60
Ethidium homodimer-2 Iodide	$EthD(I)_4$	1292.71	$EthD^{4+}$	785.11
Lanthanum Chloride	$LaCl_3$	245.26	La^{3+}	174.36
Gadolinium Chloride	$GdCl_3$	263.61	Gd^{3+}	192.71

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Abbreviations: Molecular Mass (Mol Mass)