Supporting Information

c-di-GMP induces COX-2 expression in macrophage in STING-independent manner

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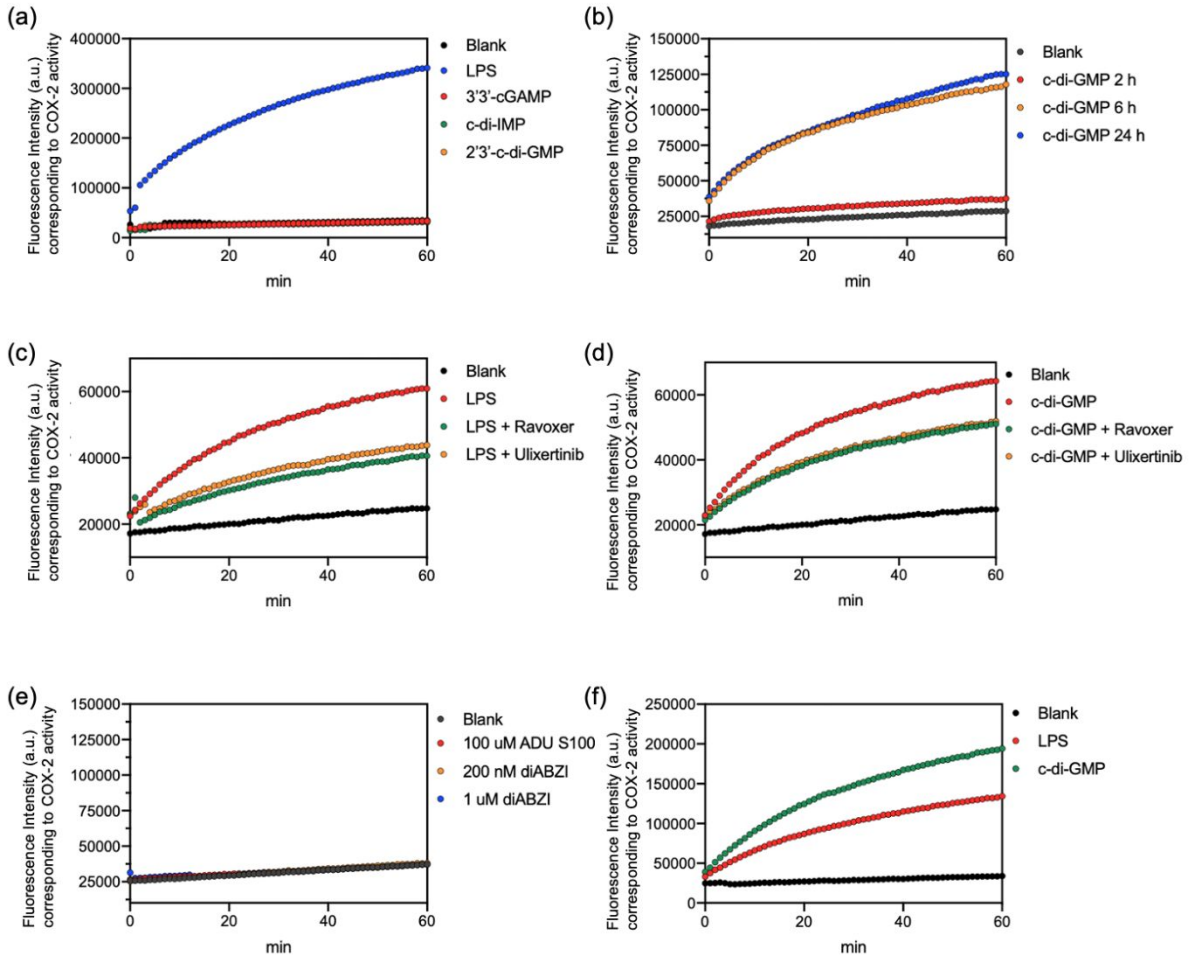
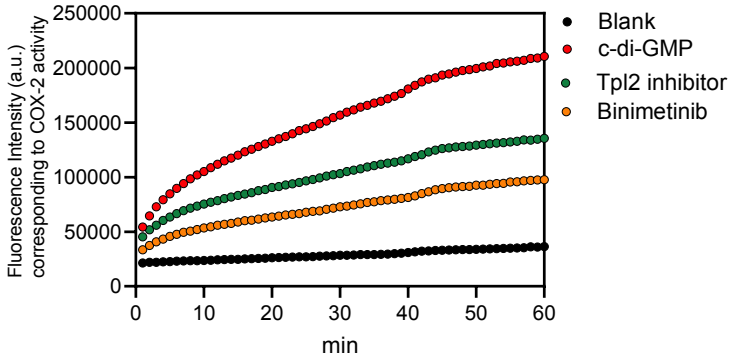


Supplementary Figure 1. Measurement of COX-2 activity of RAW macrophages upon stimulation of (**a**) LPS, 3'3'-cGAMP, c-di-IMP and 2'3'-c-di-GMP for 24 h; (**b**) c-di-GMP for 2, 6 and 24 h. Measurement of COX-2 activity of RAW macrophages pretreated with

ERK inhibitors Ravoxertinib (5 μM) and Ulixertinib (5 μM) upon stimulation of (**c**) LPS and (**d**) c-di-GMP. (**e**) Measurement of COX-2 activity of RAW macrophages upon incubation of STING activators. (**f**) Measurement of COX-2 activity of STING knock-out RAW macrophages upon stimulation of LPS and c-di-GMP.



Supplementary Figure 2. Measurement of COX-2 activity of RAW ISG cells pretreated with DMSO, Tpl2 kinase inhibitor (10 μM) or Binimetinib (10 μM) for 2 h and followed by the treatment with 100 μM c-di-GMP for 6 h.