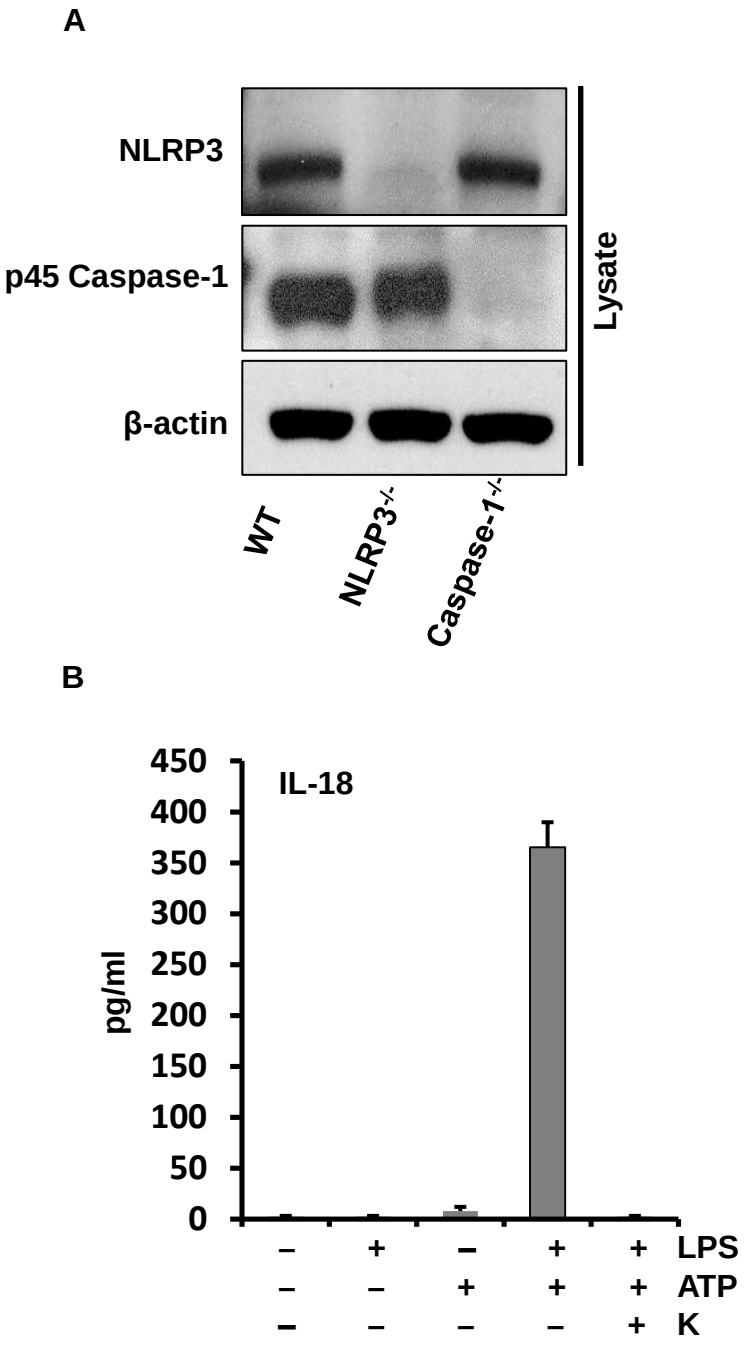

Figure S1: Confirmation of NLRP3 and caspase-1 roles in IL-18 processing. (A) Immunoblots of cell lysate confirm the absence of Nlrp3 or Caspase-1 expression in *Nlrp3*$^{-/-}$ and *Casp1*$^{-/-}$ iBMDMs.**. (B)** Monocytes were pretreated with potassium (100 mM) just prior to LPS (1 μg/ml) priming for 30 min. Supernatants were harvested after an additional 30 min of ATP (5mM) and assayed for IL-18 release.

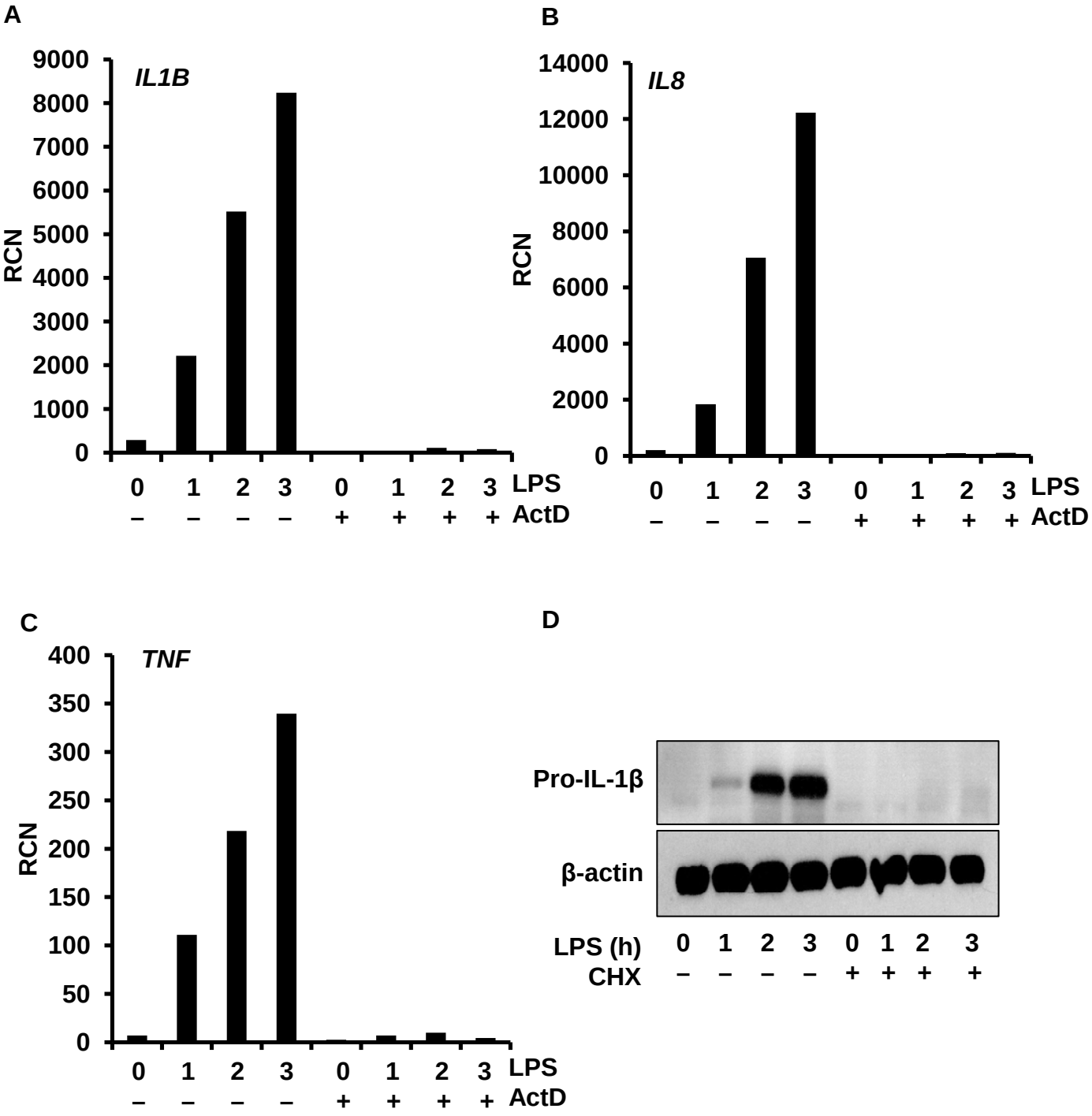

Figure S2: Actinomycin and Cycloheximide inhibit transcription and new protein translation. Monocytes were pretreated with either actinomycin D or cycloheximide for 30 min prior stimulation with LPS (1 μg/ml) for the specified time periods (0-3 hours). The effect of Actinomycin D on transcription was estimated by measuring the RNA message using RT-q-PCR **(A,B,C)**. Cell lysates were immunoblotted for the induction of proIL-1β by LPS **(D)**.

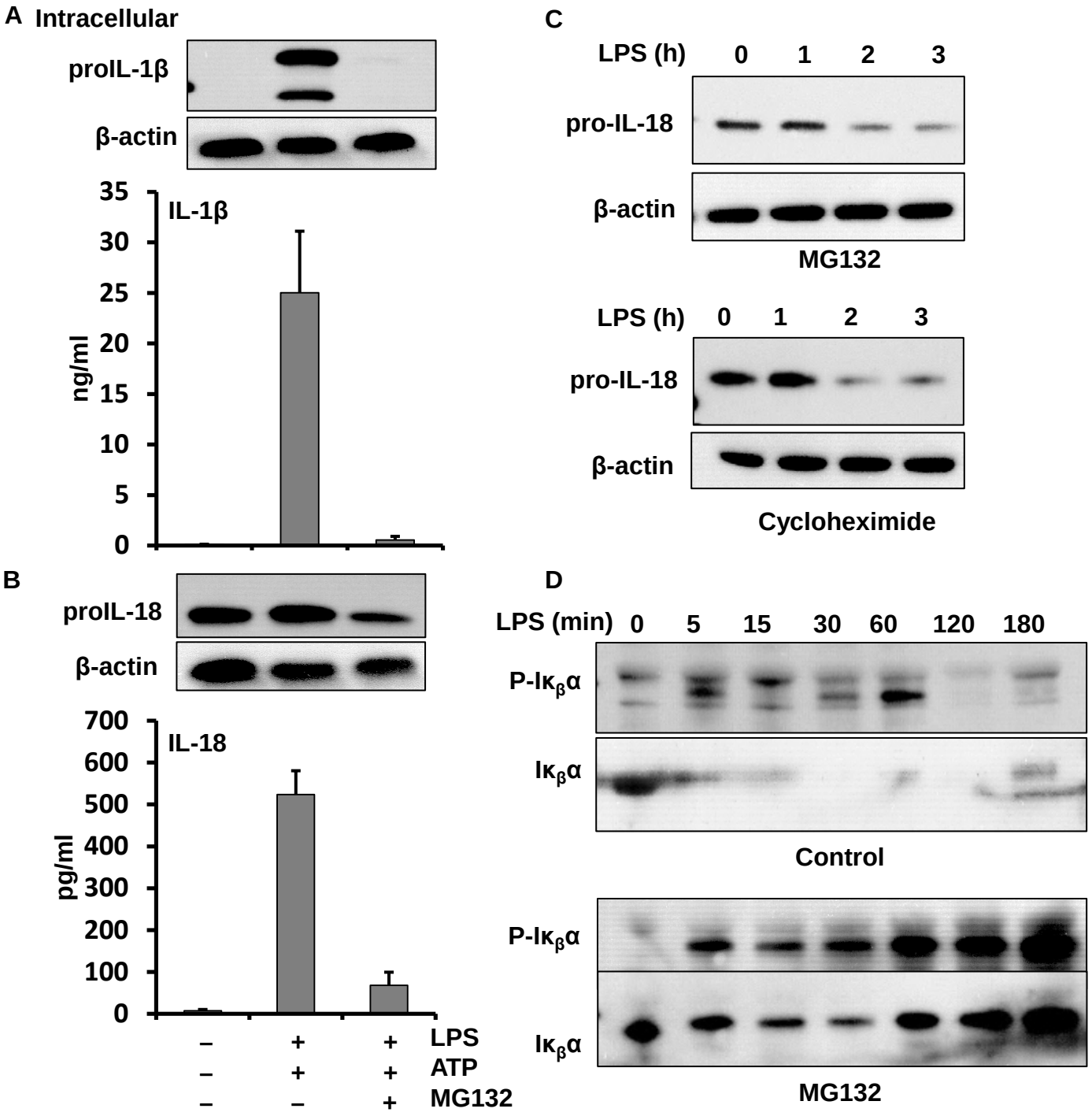

Figure S3: Proteasome inhibition blocks pro-IL-1β synthesis but also affect steady state monocyte pro-IL-18 levels after long term priming. Monocytes were pretreated with/without MG132 30 min prior to longer term LPS priming in order to allow time for proIL-1β synthesis (see Figure 1). Shown are the cell lysates by immunoblot and the cell supernatant concentrations by ELISA for **(A)** IL-1β and **(B)** IL-18. **(C)** The ability of MG132 or the protein synthesis inhibitor cycloheximide to affect the intracellular proIL-18 levels over 3 h time as detected by immunoblot. **(D)** MG132 function as a proteasome inhibitor was confirmed by its ability to prevent the LPS induced degradation while maintaining the newly induced phosphorylation of IκBα.

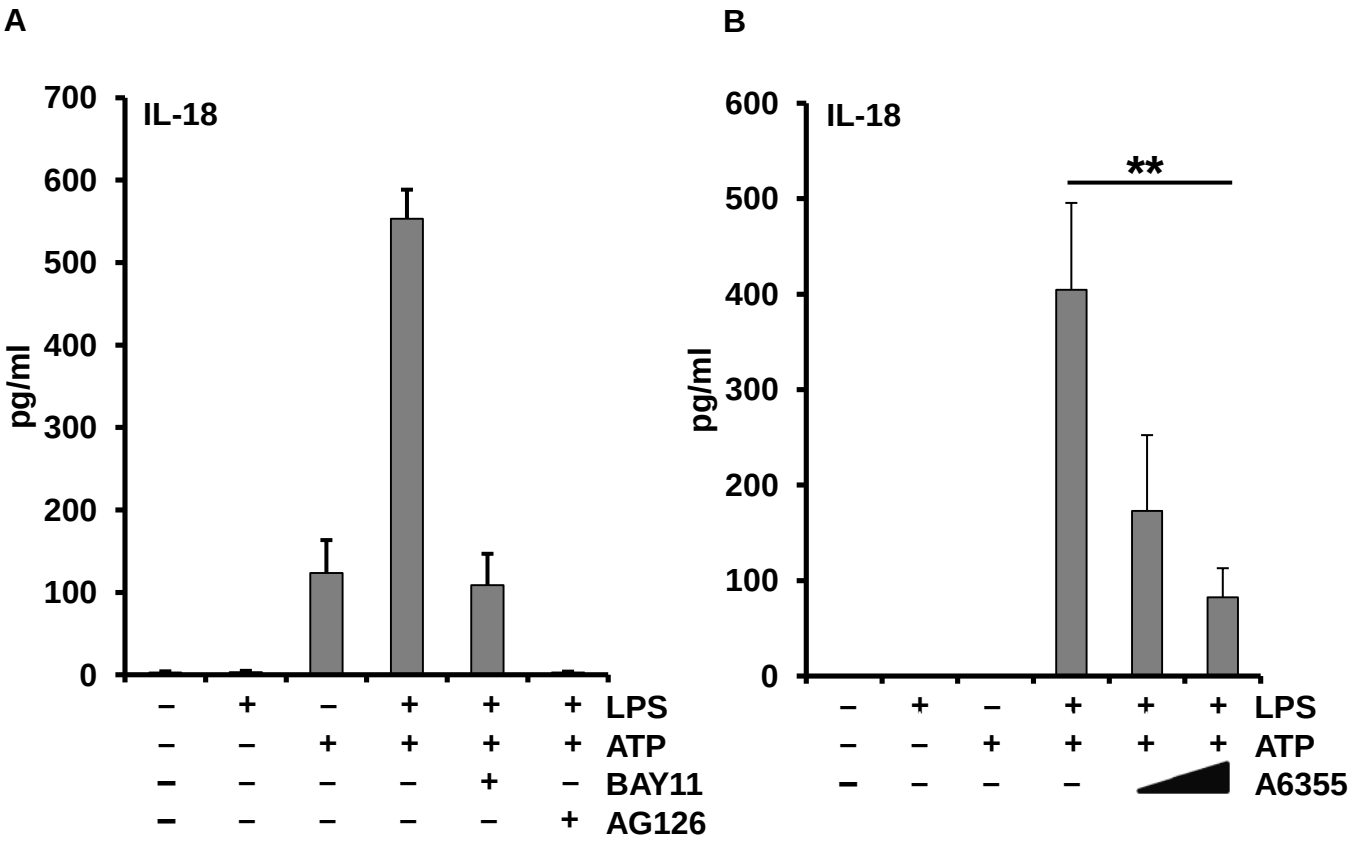

Figure S4: NFκB inhibitor BAY11 and the tyrosine kinase inhibitor AG126 and the specific ERK inhibitor A6355 prevent IL-18 release. Monocytes were pretreated with BAY11 or AG126 or A6355 (10 and 20 µM) 30 min before LPS (1 µg/ml) priming for 30 min, followed by a final 30 min of ATP (5mM). Supernatants were analyzed for IL-18 by ELISA as described, ** $p < 0.05$.