



**Extended Data Fig. 1 Cofilin-1 is a negative regulator of the NLRP3 inflammasome.**

**a**, IL-1 $\beta$  Measurements of culture supernatants from WT, *Nlrp4*-, *Mefv*-, and *Aim2*-deficient BMDMs transiently transfected with negative control siRNA (N.C.) or siRNA targeting *Cfl1*, then treated with LPS for 9h.  $n=3$ , mean + s.e.m, \*\*\* $P \leq 0.001$  and \*\*\*\* $P \leq 0.0001$  (unpaired two-tailed  $t$ -test). **b**, Immunoblot analysis with antibody to cofilin-1 in proteins IP with antibody to myc from Lys of 293T cells transiently expressing WT, the V198M variant of uncertain significance, or CAPS-associated D303G mutant NLRP3 proteins. Data are representative of three independent experiments with similar results. **c**, Structural model of the cofilin-1–NLRP3 complex highlighting the positions of eight CAPS-associated NLRP3 mutations. **d**, Predicted changes in binding affinity ( $\Delta\Delta G_{\text{binding}}$ ) between cofilin-1 and NLRP3 variants harboring CAPS-associated mutations, relative to wild-type NLRP3.