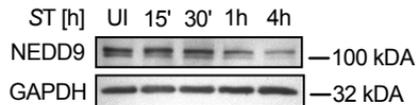
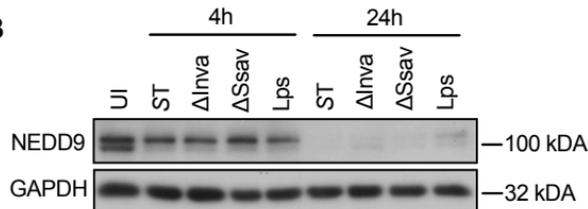


Figure S1

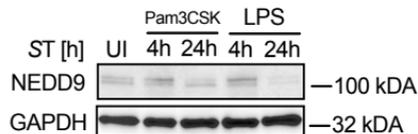
A



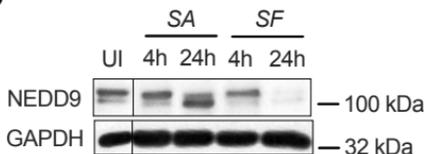
B



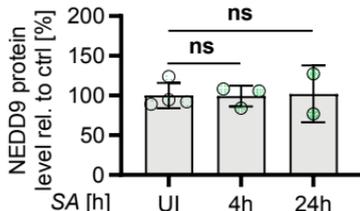
C



D



E



F

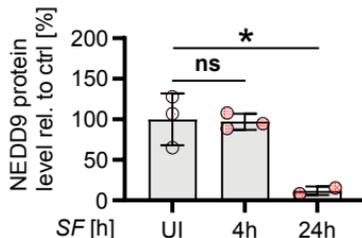


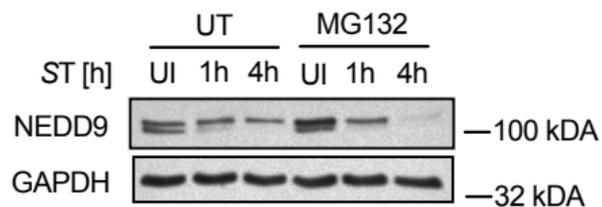
Figure S1. NEDD9 is downregulated upon infection in a virulence-independent manner.

(A) mBMDMs infected with ST for indicated time points and blotted for NEDD9 in Western blot analysis $n = 1$. (B) mBMDMs were infected with ST variants for 4h and 24h $n = 1$. (C) mBMDMs treated with PAM3CSK or LPS 100ng/ml for 4h and 24h and NEDD9 level was analyzed by Western Blotting, $n = 2$. (D) Western blot of mBMDMs infected with SA and SF at indicated time points. (E) Densitometric analysis of NEDD9 protein level normalized to GAPDH upon SA infection, Kruskal-Wallis test: no significance and (F) SF infection, $n = 3$, biological replicates, one-way ANOVA: p (UI vs. 24h) = 0.0109.

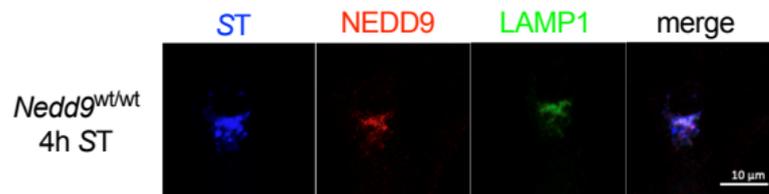
A p -value > 0.05 equals not significant (ns), * = $p \leq 0.05$, ** = $p \leq 0.01$, *** = $p \leq 0.001$, **** = $p \leq 0.0001$.

Figure S2

A



B



C

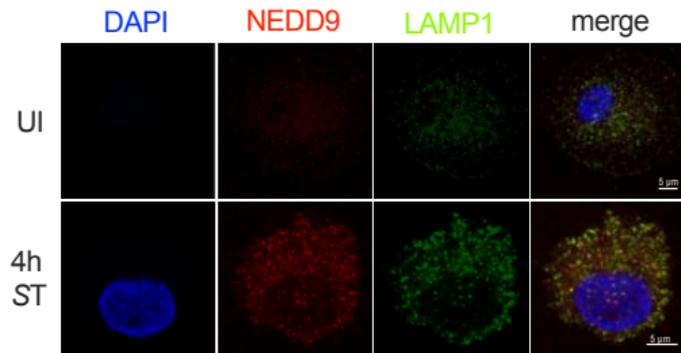
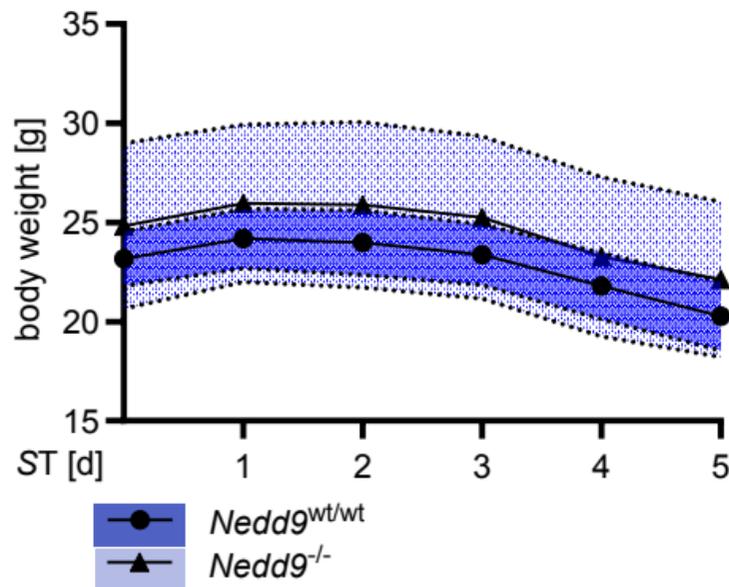


Figure S2. Increased phagolysosomal activity upon loss of NEDD9.

(A) Infection of *Nedd9*^{wt/wt} mBMDMs with ST and parallel treatment with MG132 (50 μM) followed by Western blotting, n = 3, biological replicates. (B) Infection of *Nedd9*^{wt/wt} mBMDMs with ST followed by immunofluorescence staining of ST (blue), NEDD9 (red) and LAMP1 (green), n = 10, biological replicates. (C) Representative confocal microscopy images of human macrophages uninfected and infected for 4 hours with ST and stained for NEDD9 (red) and LAMP1 (green).

Figure S3

A



B

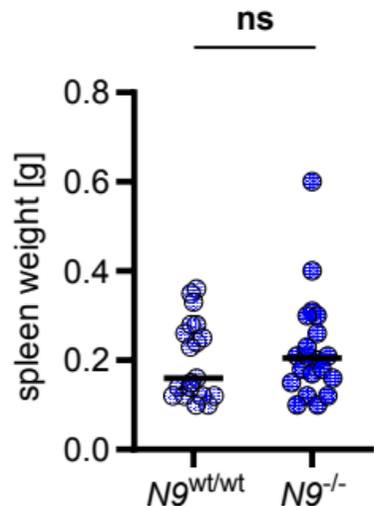
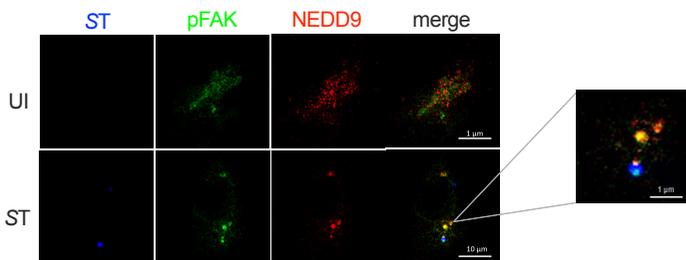


Figure S3. Bodyweight reduction and spleen weight are not affected by the loss of NEDD9.

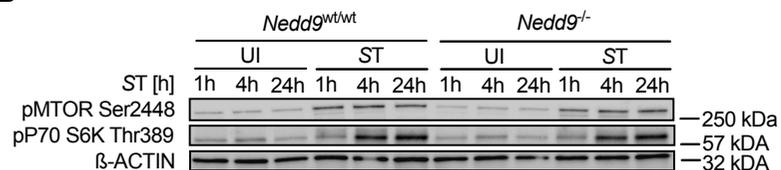
Infection of *Nedd9*^{wt/wt} and *Nedd9*^{-/-} mice with ST for 4 days. **(A)** Bodyweight of *Nedd9*^{wt/wt} and *Nedd9*^{-/-} mice throughout ST infection. *Nedd9*^{wt/wt} n = 6, *Nedd9*^{-/-} n = 8, biological replicates. **(B)** Spleen weight of *Nedd9*^{wt/wt} and *Nedd9*^{-/-} mice 4 days post ST infection. *Nedd9*^{wt/wt} n = 19, *Nedd9*^{-/-} n = 20, biological replicates, Mann-Whitney test: no significance.

Figure S4

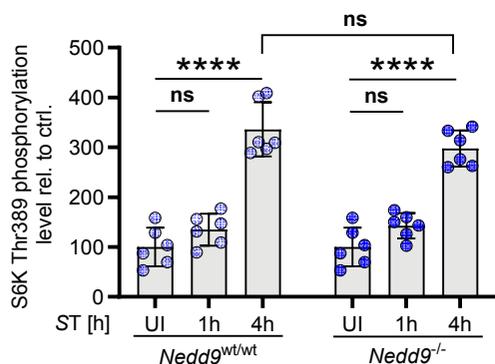
A



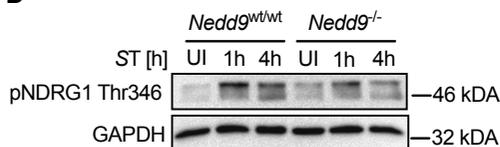
B



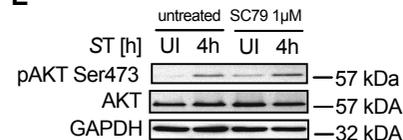
C



D



E



F

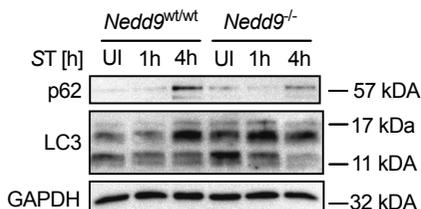


Figure S4. Increased phagolysosomal capacities by reduced mTOR/p62 signaling.

(A) IF Triplestaining of pFAK, NEDD9 and ST in *Nedd9^{wt/wt}* mBMDMs uninfected and ST4h. (B) Western blot analysis of phospho-mTOR and phospho-S6K, n = 3, biological replicates. (C) Densitometric analysis of Western blots showing phosphorylated S6 kinase (S6K), 2-way ANOVA: p (*Nedd9^{wt/wt}* UI vs. ST 4h) < 0.0001, p (*Nedd9^{-/-}* UI vs. ST 4h) < 0.0001. (D) Western blot analysis of phospho-NDRG-1, n = 3, biological replicates. (E) Western blot analysis of ST infected *Nedd9^{-/-}* mBMDMs untreated and treated for 1h and 4h with 1μM AKT activator SC-79 and blotted for pAKTSer473 and total AKT, n = 3, biological replicates. (F) Western blot analysis of p62 and LC3, n = 3, biological replicates.