

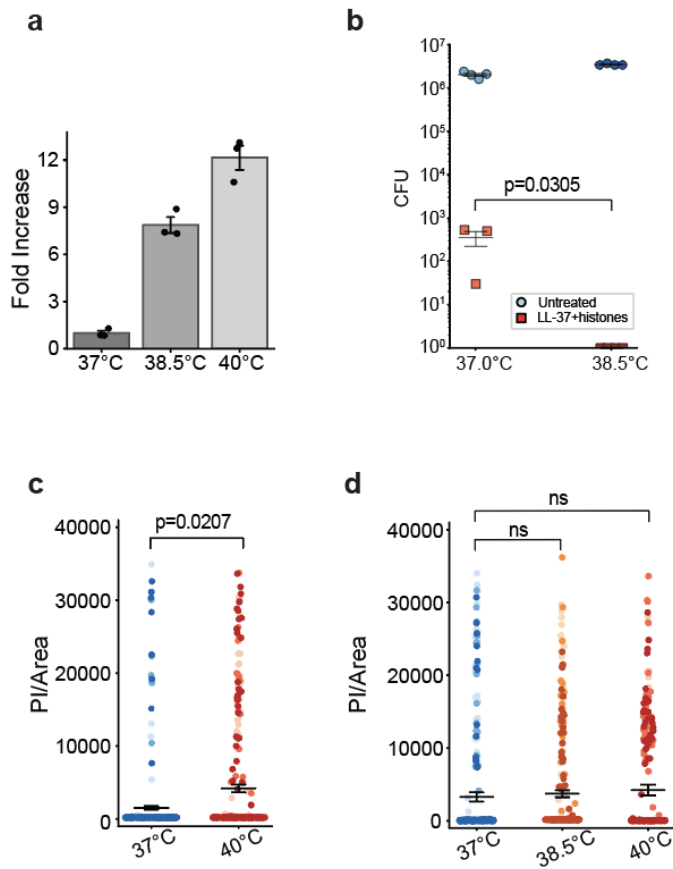
# **Fever enhances host bacterial defence while limiting mitochondrial damage**

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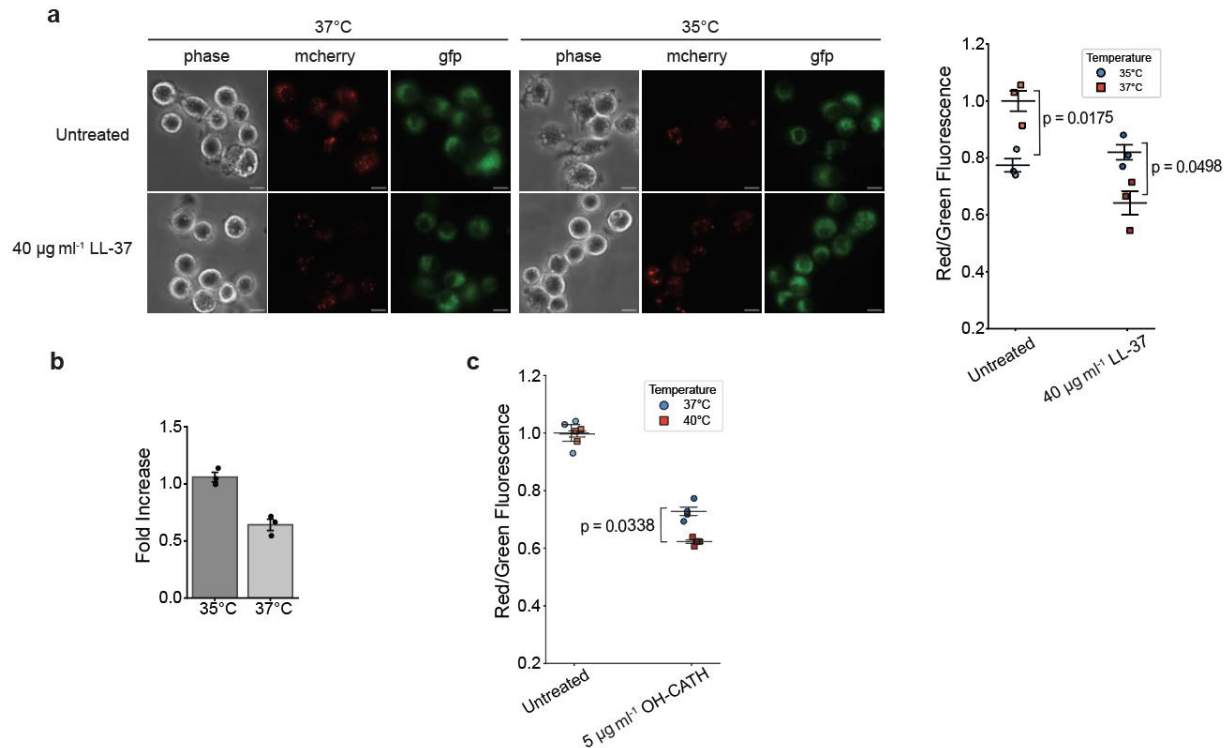
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Extended Data Figures 1-2

Extended Data Tables 1-3



**Extended Data Fig. 1 | Quantification of propidium iodide (PI) intensity and CFU at different treatments. (a)** Fold increase of PI fluorescence of increasing temperature in dual treated 5  $\mu\text{g ml}^{-1}$  histones and 10  $\mu\text{g ml}^{-1}$  LL-37 normalized by 37°C. **(b)** CFUs performed at indicated temperatures for 5  $\mu\text{g ml}^{-1}$  whole histone and 20  $\mu\text{g ml}^{-1}$  LL-37 dual treatment for 4 h. **(c)** PI quantification for *E. coli* MG1655 treated with 5  $\mu\text{g ml}^{-1}$  histones and 5  $\mu\text{g ml}^{-1}$  LL-37, **(d)** and 20  $\mu\text{g ml}^{-1}$  LL-37 alone at indicated temperatures. Black bar indicated the mean and error bars represented SEM from three replicates. P-values greater than 0.05 are denoted as non-significant (ns)



**Extended Data Fig. 2 | Representative fluorescence microscopy images and quantification of JC-1 red/green fluorescence ratio under different treatments. (a)** Representative fluorescence microscopy images of J774.1 macrophages with treatment of 40 µg ml<sup>-1</sup> LL-37 at 37°C and 35°C and quantification of JC-1 red/green fluorescence ratio. Scale bar = 10 µm. **(b)** Fold changes of mitochondrial activity for 40 µg ml<sup>-1</sup> LL-37 normalized by untreated at 35°C and 37°C. **(c)** Quantification of JC-1 red/green fluorescence ratio of 5 µg ml<sup>-1</sup> OH-CATH treated J774.1 for 1 h at 37°C and 40°C. Black bar indicated the mean and error bars represented SEM from three replicates. P-values greater than 0.05 are denoted as non-significant (ns).

Treatments	37°C	40°C
5 $\mu\text{g ml}^{-1}$ LL-37	1.67%	4.67%
5 $\mu\text{g ml}^{-1}$ histones + 5 $\mu\text{g ml}^{-1}$ LL-37	5.33%	23.76%
40 $\mu\text{g ml}^{-1}$ LL-37	33.65%	66.67%
10 $\mu\text{g ml}^{-1}$ H1 + 2 $\mu\text{g ml}^{-1}$ LL-37	1.33%	18.00%
400 $\mu\text{g ml}^{-1}$ H1	14.67%	15.00%

**Extended Data Table 1 | Percentage of cells with PI entry treated by histones, LL-37, histone H1 or combined treatments at physiological or febrile temperature.**

Treatments	37°C	38.5°C	40°C
5 µg ml <sup>-1</sup> histones + 10 µg ml <sup>-1</sup> LL-37	3.03%	18.52%	32.32%
20 µg ml <sup>-1</sup> LL-37	17.69%	23.67%	28.90%
100 µg ml <sup>-1</sup> histones	34.67%	40.33%	57.33%

**Extended Data Table 2 | Percentage of cells with PI entry treated by histones, LL-37, and combined treatment across febrile temperature range.**

Treatments	20°C	25°C	30°C	35°C	40°C	42°C
8 µg ml <sup>-1</sup> OH-CATH	60.00%	32.00%	46.67%	56.58%	66.67%	62.67%
0.5 µg ml <sup>-1</sup> Pelteobagrín	60.00%	84.67%	56.00%	41.33%	-	-
40 µM Magainin-2	64.33%	54.73%	42.18%	29.00%	-	-

**Extended Data Table 3 | Percentage of cells with PI entry following treatment by cold blood animals' peptides treatment under indicated temperatures.**