

## SUPPLEMENTARY INFORMATION

### Control of bacterial cell wall autolysins by peptidoglycan crosslinking mode

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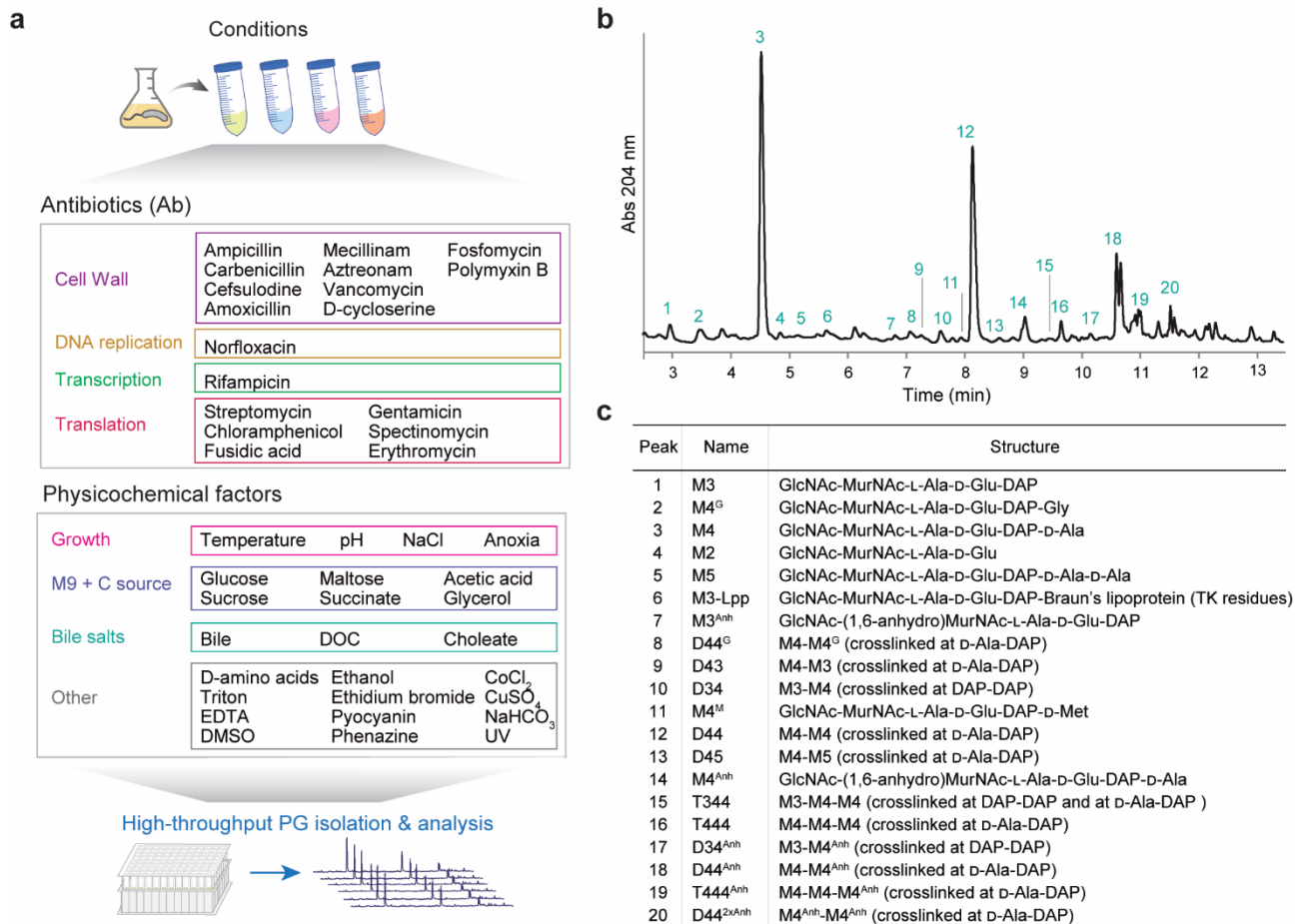
**Running title:** Autolysin inhibition by peptidoglycan crosslinking

**Keywords:** cell wall, *Vibrio cholerae*, peptidoglycan, LD-crosslink, anhydromuropeptides, lytic transglycosylases

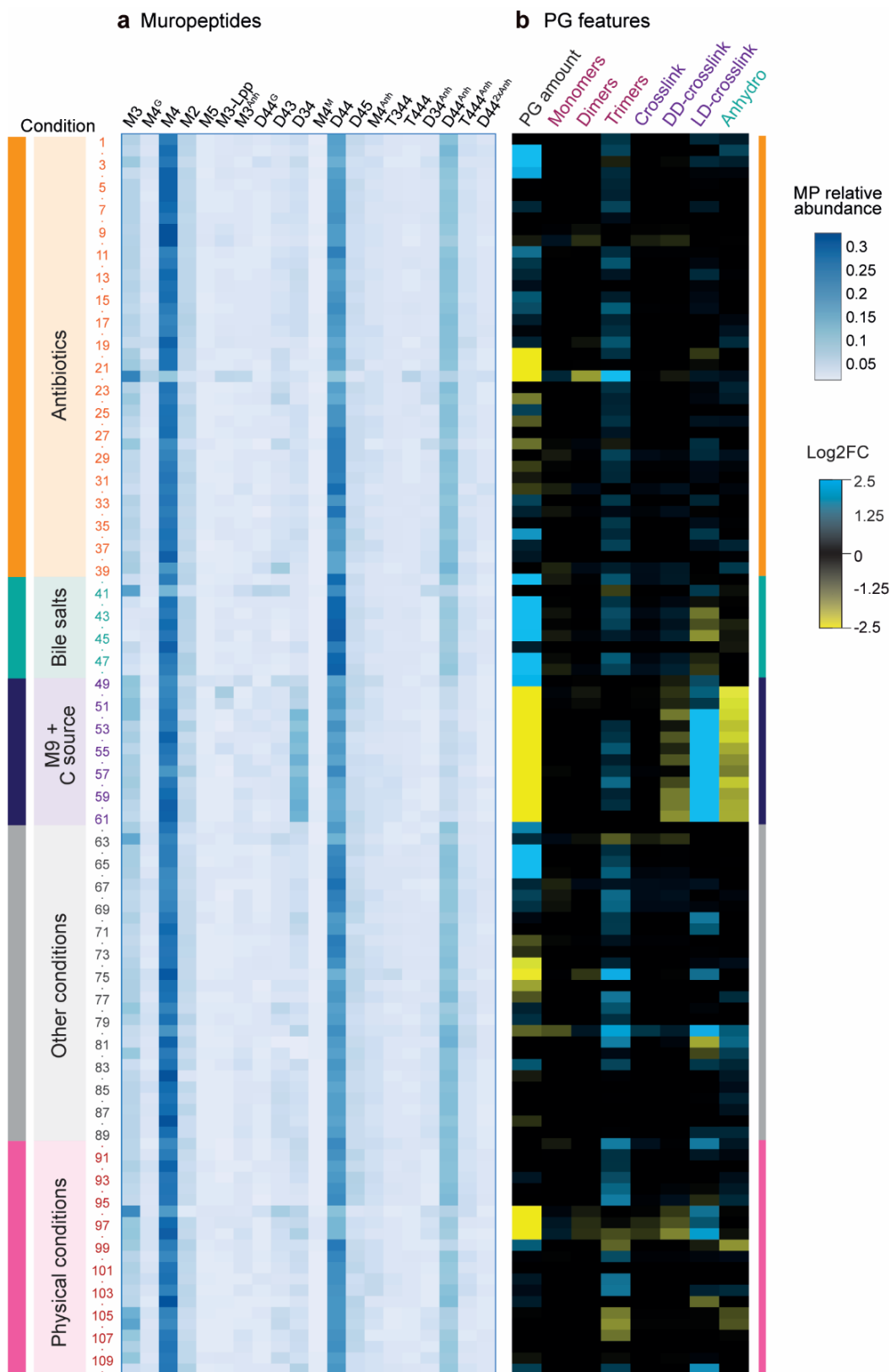
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## Supplementary Figures

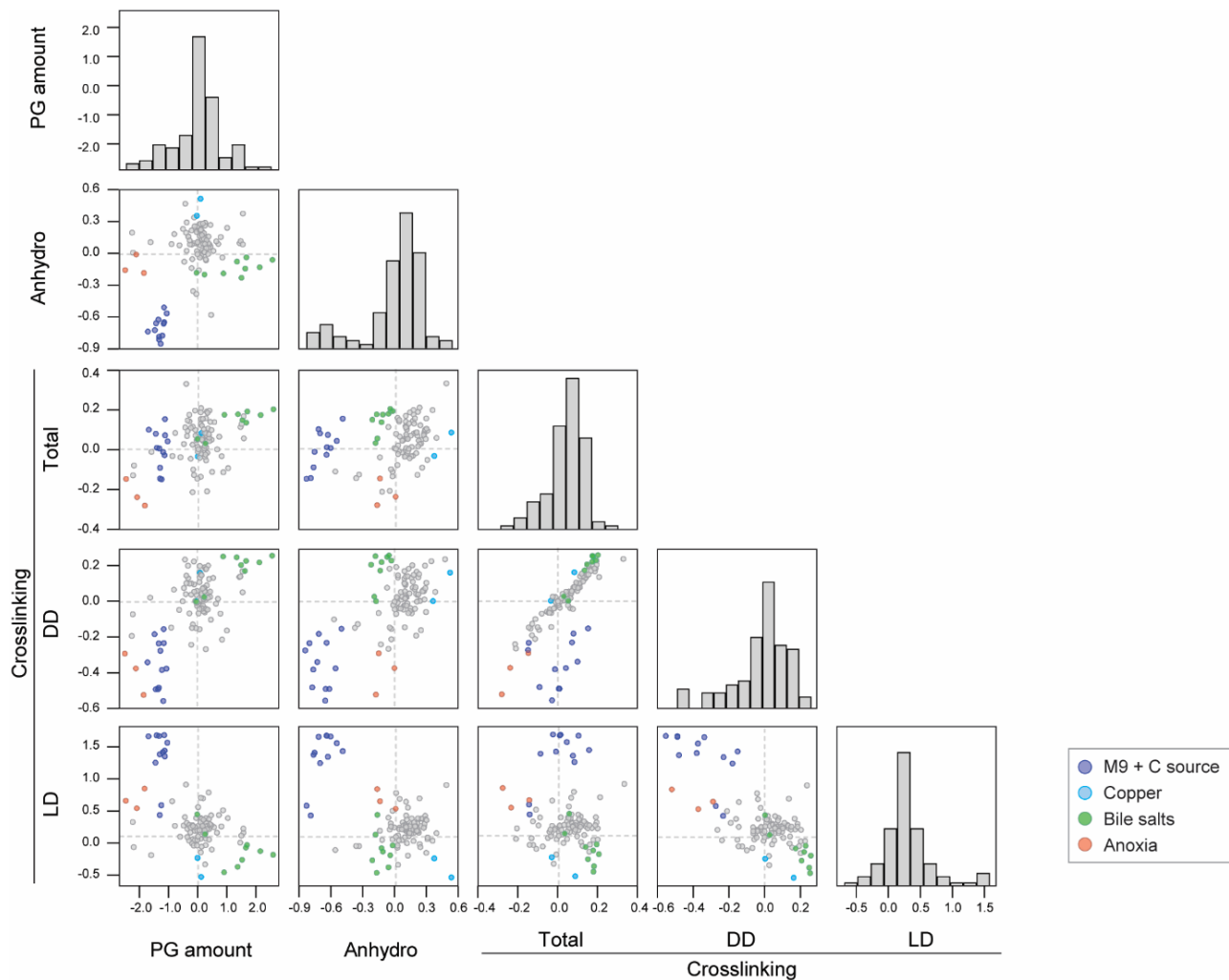


**Supplementary Figure 1. Screening of *V. cholerae*'s peptidoglycan plasticity across different conditions.** **a.** Wild type *V. cholerae* was exposed to sub-MIC concentrations of the indicated antibiotics or stress conditions (panels on the left). Several substances were tested at different concentrations such that a total of 110 different growth conditions were surveyed. Samples were processed for PG isolation and analysis using a filter-based high-throughput preparation method. **b.** Representative chromatogram of wild type *V. cholerae* strain. Identified peaks are listed. **c.** Table of muuropeptides identified in **b**, confirmed by mass spectrometry. GlcNAc: *N*-acetyl glucosamine; MurNAc: *N*-acetyl muramic acid; (1,6-anhydro)MurNAc: terminal 1,6-anhydro-*N*-acetyl muramic acid; L-Ala: L-alanine; D-Glu: D-glutamic acid; DAP: *meso* diaminopimelic acid; D-Ala: D-alanine; D-Met: D-methionine; Gly: glycine; Lpp: Braun's lipoprotein.

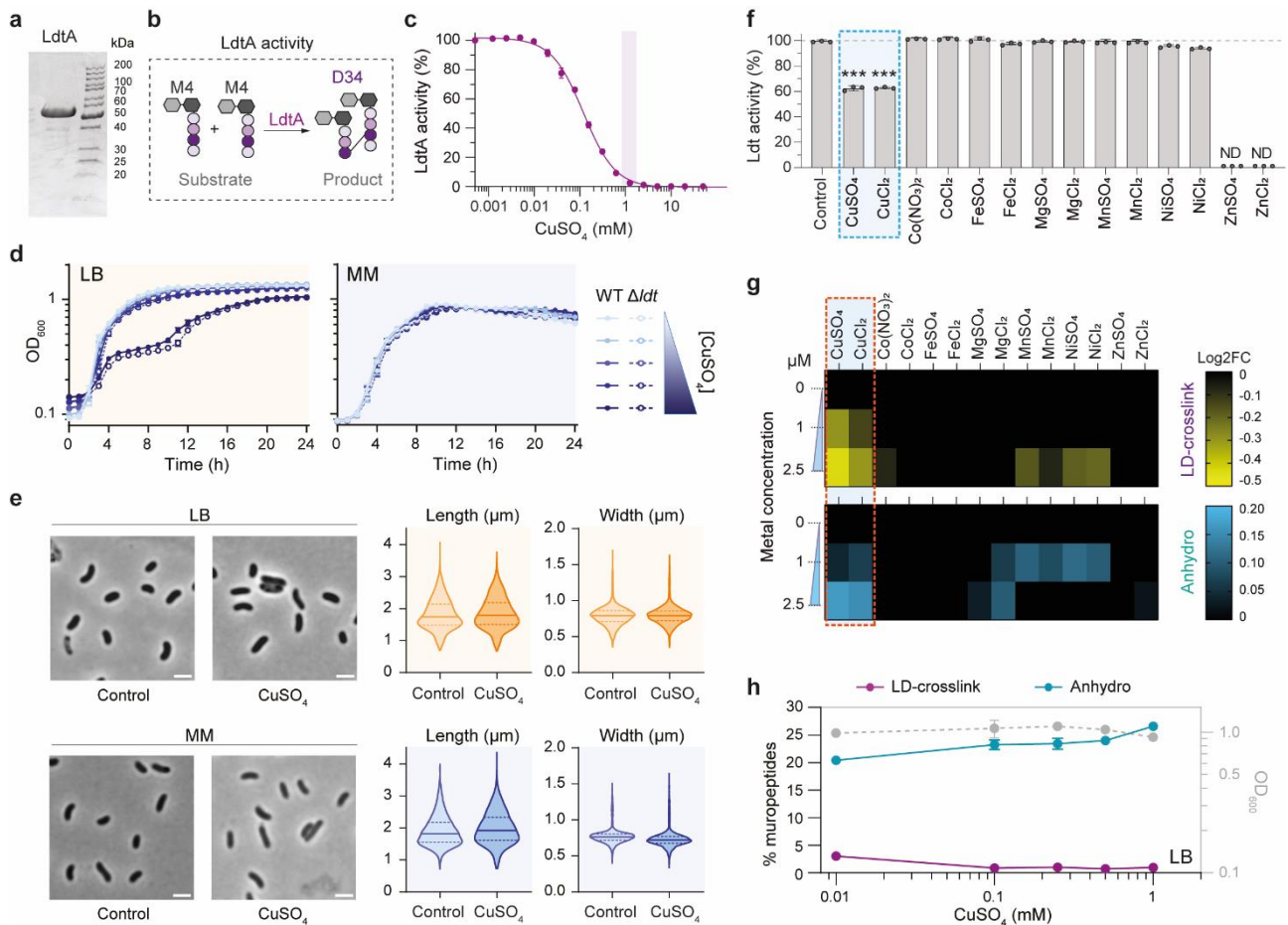


**Supplementary Figure 2. Peptidoglycan analysis of *V. cholerae* grown under different conditions. a.** Heatmap representing the relative abundance of the identified muropeptides

(MP) for all tested conditions (Suppl. Data 1). **b.** Heatmap representing the Log<sub>2</sub>FC calculated for the main peptidoglycan (PG) features. All values are mean of 3 biological replicates. M9+C source: M9 minimal medium supplemented with carbon sources. Details and source data are provided in Supplementary Data 1.



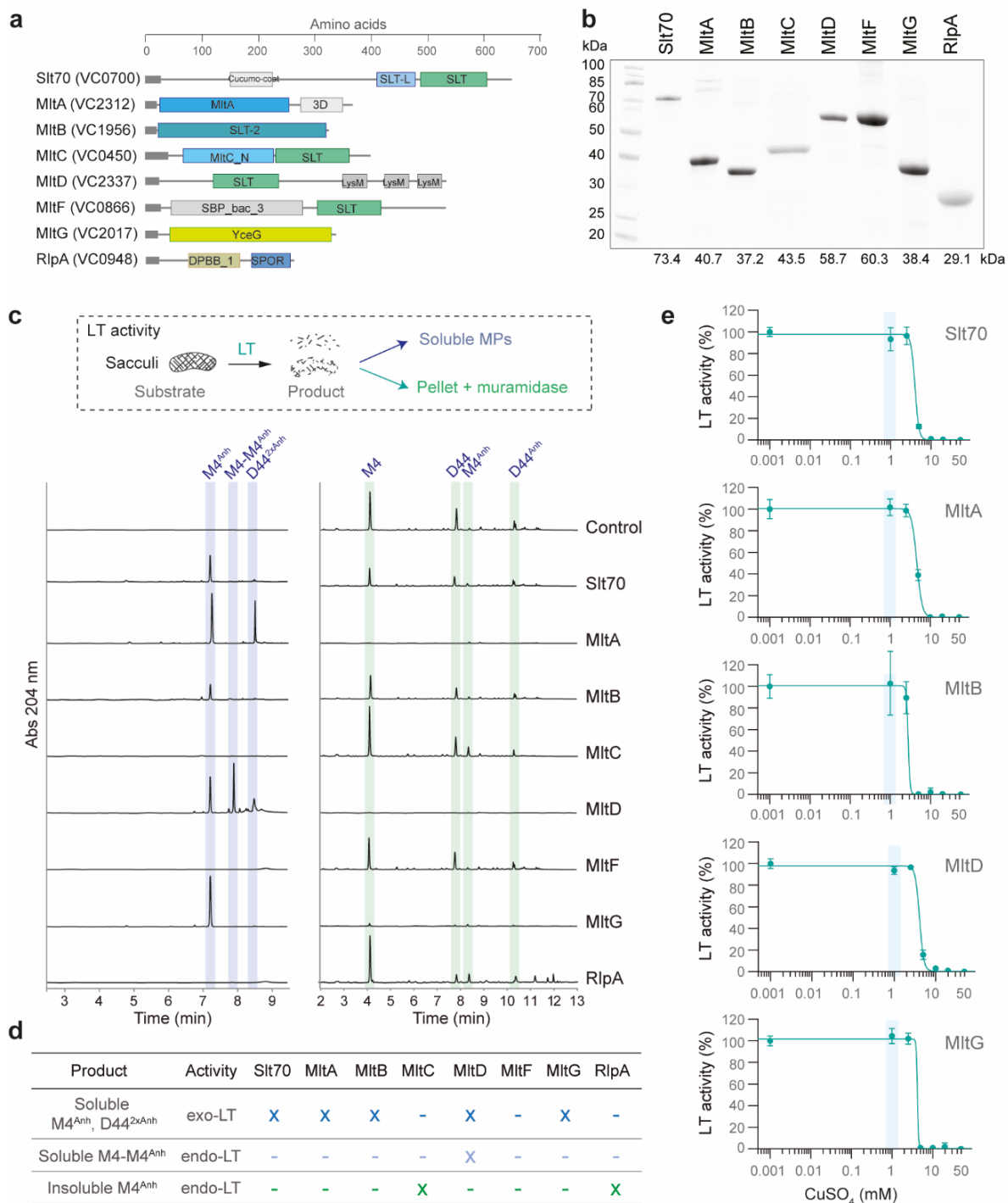
**Supplementary Figure 3. Scatter matrix for the main peptidoglycan features for *V. cholerae* grown under the tested conditions.** Scatter plots representing the Log<sub>2</sub>FC of main peptidoglycan (PG) features: relative PG amount, anhydromuropeptide levels, crosslinking (total and type). Clusters of conditions of interest are highlighted. Values shown in scatter plots are the mean of 3 biological replicates. Histograms showing the distribution of samples for every dimension are represented in the diagonal. Source data are provided in Supplementary Data 1.



**Supplementary Figure 4. Inhibition of *V. cholerae* LD-transpeptidase by copper.** **a.** Purified LdtA from *V. cholerae*, the LD-transpeptidase which produces LD-crosslinks. The molecular weight of the purified His-tagged protein is predicted to be 58.8 kDa. **b.** Schematic diagram of the LdtA in vitro reaction: LdtA converts M4 monomers into LD-crosslinked D34 dimers. **c.** Relative LdtA activity at different copper concentrations. Working concentration in bacterial cultures in LB is highlighted (1 mM). In vitro assays were performed in triplicate. Data are presented as mean values +/- standard deviation. **d.** Growth of *V. cholerae* WT and  $\Delta ldt$  mutant in LB with 0.5-2 mM  $\text{CuSO}_4$  and MM with 1-10  $\mu\text{M}$   $\text{CuSO}_4$ . Growth curves were performed in triplicate. Data are presented as mean values +/- standard deviation. **e.** Representative phase contrast images and violin plots of the length and mean width of *V. cholerae* WT grown in LB (top) or MM (bottom) in the presence or absence of  $\text{CuSO}_4$  at 1

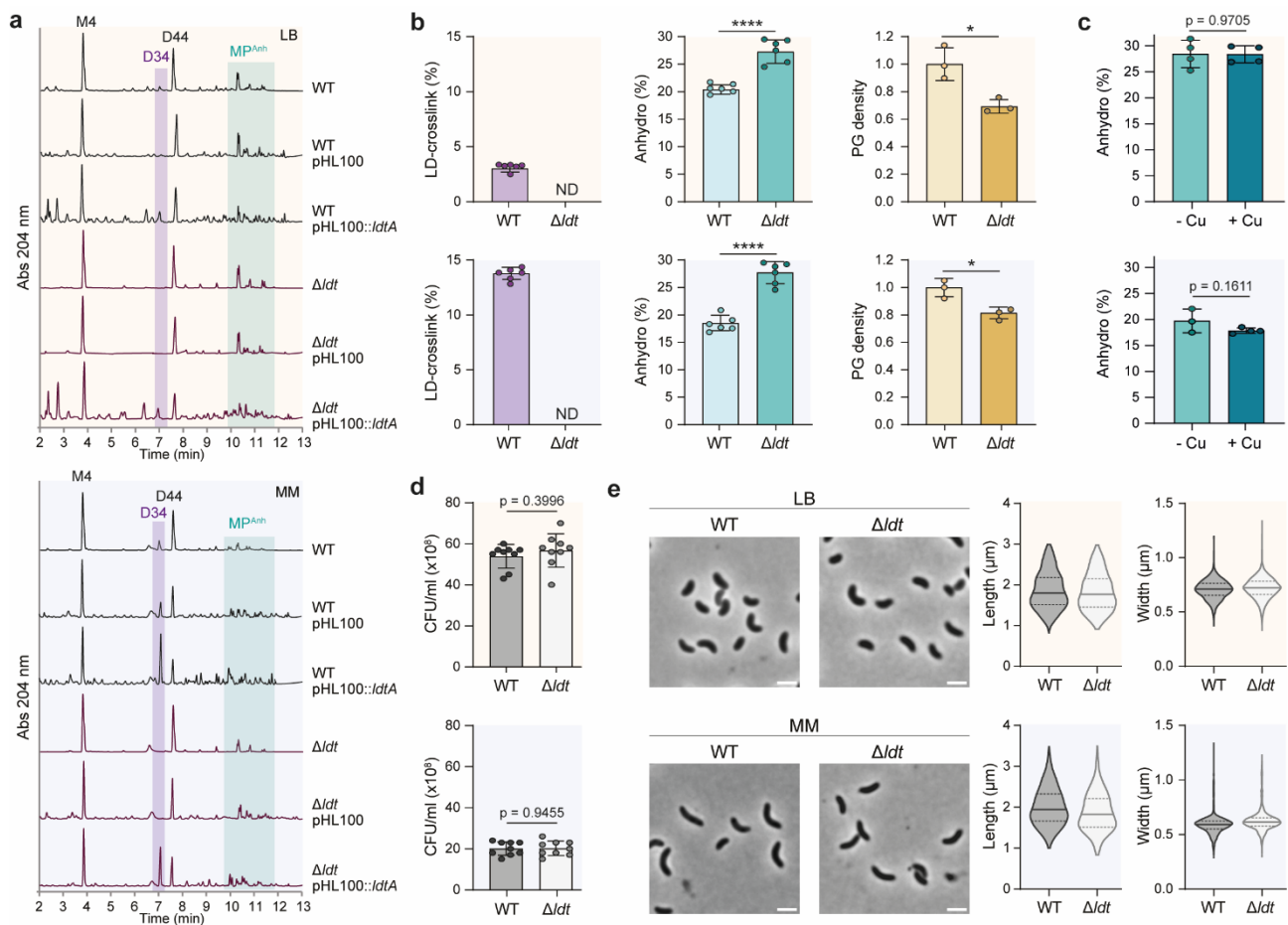
mM (in LB) or 5  $\mu$ M (in MM). Scale bar: 2  $\mu$ m. Samples size: LB control, n = 6493; LB CuSO<sub>4</sub>, n = 4144; MM control, n = 4724; MM CuSO<sub>4</sub>, n = 3821. **f.** Relative LdtA activity in presence of 0.1 mM of different metal salts. In vitro assays were performed in triplicate. Data are presented as mean values +/- standard deviation. Statistical significance was determined using unpaired t-tests, with an alpha level of 0.05. Two-tailed p values are reported in the Source Data file. ND, not detected; \*\*\*, p <0.001. **g.** Effect of different metal salts on *V. cholerae* PG features in vivo. Heatmaps represent the mean Log<sub>2</sub>FC calculated for LD-crosslink and anhydromuropeptide levels in the PG of *V. cholerae* cultures grown in MM with 1 or 2.5  $\mu$ M of respective metal salt. PG analyses were performed in triplicate. **h.** Concentration-dependent effect of copper on LD-crosslink and anhydromuropeptide levels in the PG of *V. cholerae* grown in LB. Assays were performed in quintuplicate. Data are presented as mean values +/- standard deviation. Source data are provided as a Source Data file.





**Supplementary Figure 5. In vitro lytic transglycosylase activity.** **a.** Domain architecture of the lytic transglycosylases (LTs) in *V. cholerae*. **b.** Purified LTs from *V. cholerae*. Predicted molecular weight of the purified His-tagged proteins is indicated at the bottom. **c.** Schematic diagram of in vitro assay used to study the activity of *V. cholerae*'s LTs. Sacculi from *V. cholerae* WT grown in LB was used as substrate. Upon digestion with the LTs, the soluble

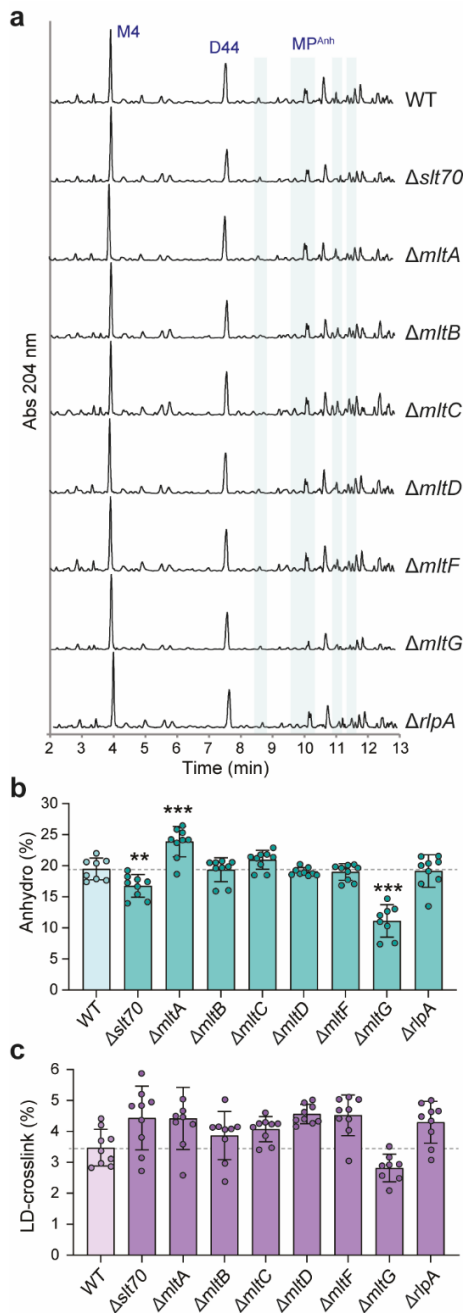
products were directly analyzed by LC, and the insoluble pellets were further digested with muramidase prior to LC analysis. Major products are highlighted in the chromatograms. **d.** Summary table of the LT activities of each tested enzyme. **e.** Relative LT activity at different copper concentrations of the LTs. Working concentration in bacterial cultures in LB is highlighted (1 mM). In vitro assays were performed in triplicate. Data are presented as mean values +/- standard deviation. Source data are provided as a Source Data file.



**Supplementary Figure 6. Characterization of the *V. cholerae*  $\Delta$ ldt mutant. a.**

Representative chromatograms obtained from PG of *V. cholerae* WT,  $\Delta$ ldt mutant and complemented strains grown in LB (top) or MM (bottom). LD-crosslinked D34 muropeptide and anhydromuropeptides (MP<sup>Anh</sup>) are indicated. **b.** Relative amount of LD-crosslinked muropeptides, anhydromuropeptides and PG density of *V. cholerae* WT and  $\Delta$ ldt strains grown in LB (top) or MM (bottom). PG analyses were performed in 6 replicates (triplicates for PG density). Data are presented as mean values +/- standard deviation. Statistical significance was determined using unpaired t-tests, with an alpha level of 0.05. Two-tailed p values are reported in the Source Data file. ND, not detected; \*, p < 0.05; \*\*\*\*, p < 0.0001. **c.** Relative amount of anhydromuropeptides in the PG of the *V. cholerae*  $\Delta$ ldt mutant in the presence of CuSO<sub>4</sub> 1 mM CuSO<sub>4</sub> in LB (top) or 5 μM CuSO<sub>4</sub> in MM (bottom). PG analyses

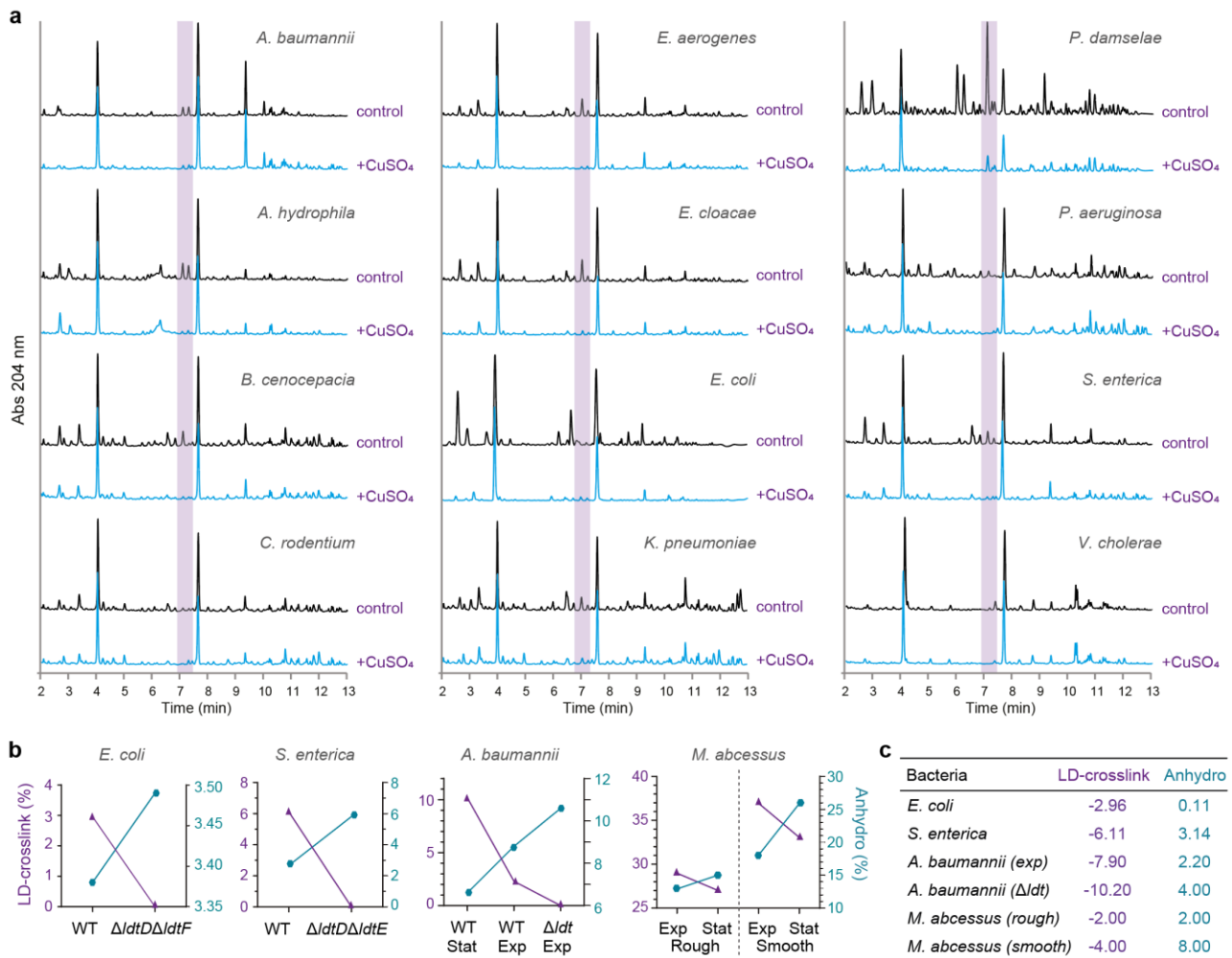
were performed in quadruplicates. Data are presented as mean values +/- standard deviation. Statistical significance was determined using unpaired t-tests, with an alpha level of 0.05. Two-tailed p values are reported. **d.** CFU/ml of *V. cholerae* WT and  $\Delta/dt$  mutant cultures grown overnight in LB (top) or MM (bottom). 9 replicates were analyzed in the viability assays. Data are presented as mean values +/- standard deviation. Statistical significance was determined using unpaired t-tests, with an alpha level of 0.05. Two-tailed p values are reported. **e.** Representative phase contrast images and violin plots of the length and mean width of *V. cholerae* WT and  $\Delta/dt$  mutant cells grown in LB (top) or MM (bottom). Scale bar: 2  $\mu$ m. Samples size: WT LB, n = 1807;  $\Delta/dt$  LB, n = 1630; WT MM, n = 1418;  $\Delta/dt$  MM, n = 1264. Source data are provided as a Source Data file.



**Supplementary Figure 7. Peptidoglycan analysis of *V. cholerae* lytic transglycosylase mutants.** **a.** Representative chromatograms of the PG of *V. cholerae* WT and  $\Delta$ LT strains grown in LB. Anhydromuropeptides (MP<sup>Anh</sup>) are indicated in green. **b.** Relative amount of anhydromuropeptides in the PG of *V. cholerae* WT and LT mutants grown in LB. **c.** Relative amount of LD-crosslink in the PG of *V. cholerae* WT and  $\Delta$ LT strains grown in LB. PG analyses were performed in 9 replicates. Data are presented as mean values +/- standard deviation. Statistical significance was determined using unpaired t-tests, with an alpha level

of 0.05. Two-tailed p values are reported in the Source Data file. \*\*, p <0.01; \*\*\*, p <0.001.

Source data are provided as a Source Data file.

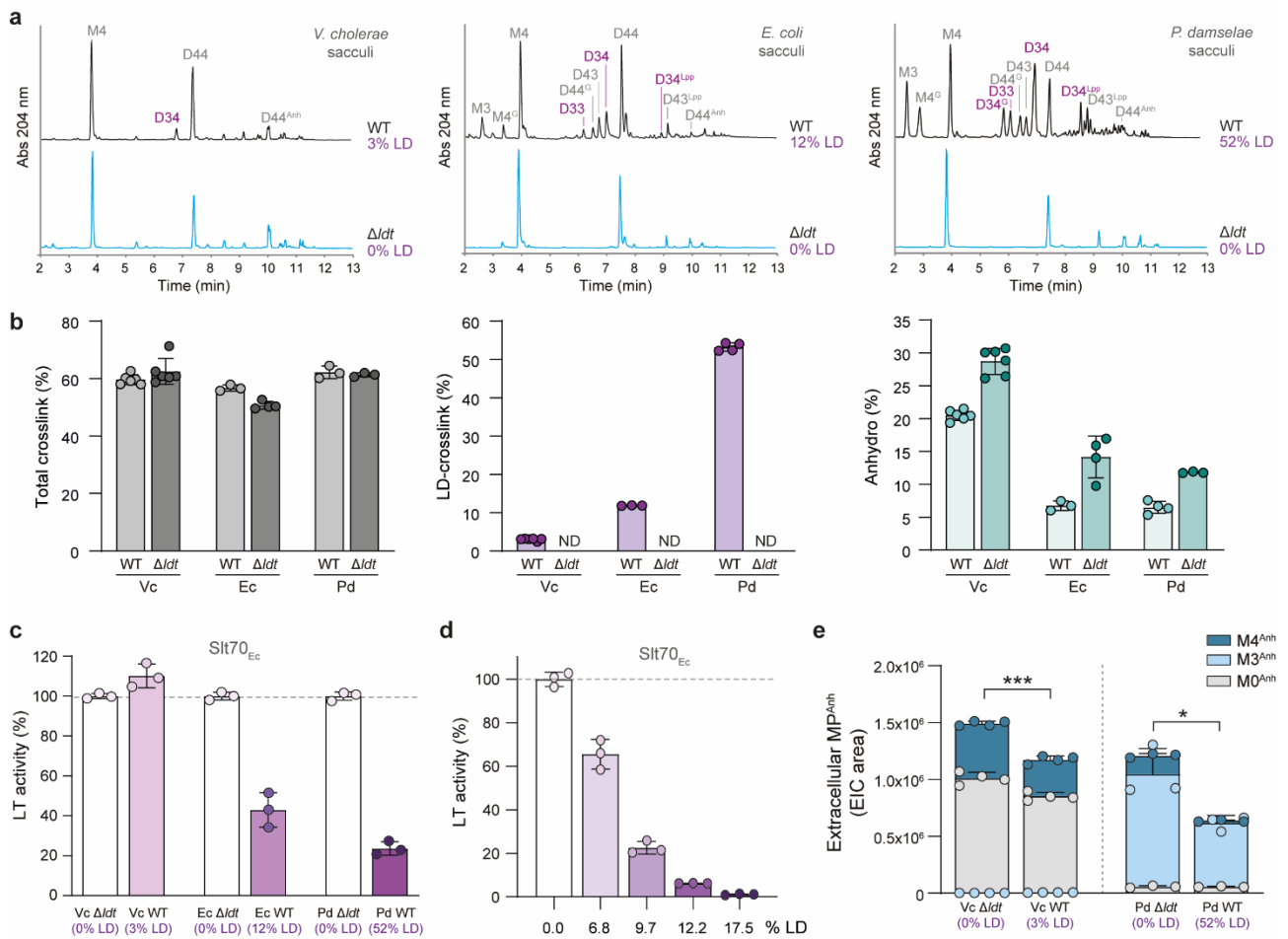


**Supplementary Figure 8. Effect of inhibition of LD-transpeptidases by copper in different bacterial species.** **a.** Representative chromatograms of different bacterial species (*Acinetobacter baumannii*, *Aeromonas hydrophila*, *Burkholderia cenocepacia*, *Citrobacter rodentium*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Photobacterium damsela*, *Pseudomonas aeruginosa*, *Salmonella enterica* and *Vibrio cholerae*) grown in absence (control) or presence of 1 mM CuSO<sub>4</sub>. All bacteria were grown in LB, except for *P. damsela* which was grown in TSB. **b.** Inverse correlation between relative amounts of LD-crosslink and anhydromuropeptides observed for different bacteria in the literature<sup>1-4</sup>. Exp, exponential phase; Stat, stationary phase. **c.** Calculated

change in the relative amounts of LD-crosslink and anhydromuropeptides from the data in

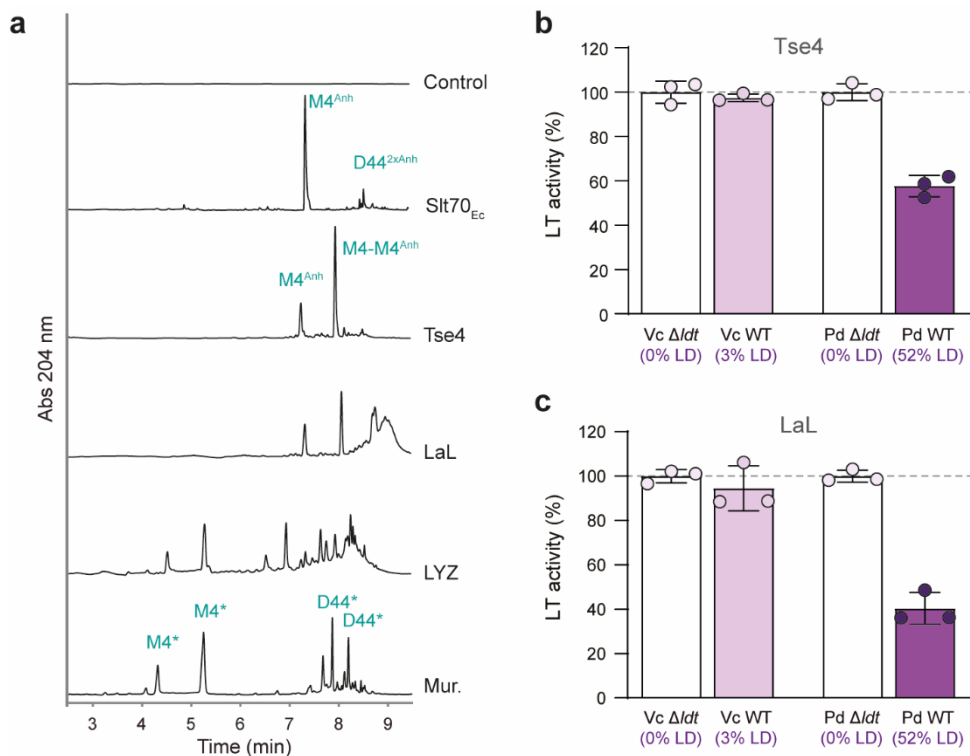
**b.** Source data are provided as a Source Data file.



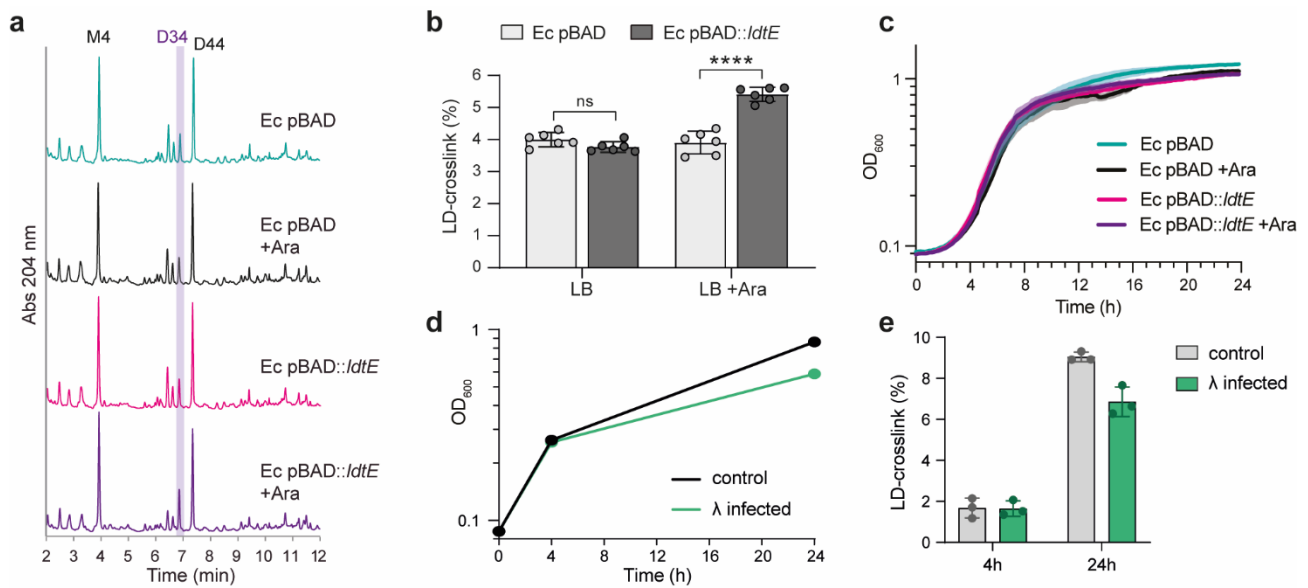


**Supplementary Figure 9. LD-crosslinks inhibit the activity of endogenous lytic transglycosylases.** **a.** Representative chromatograms of *V. cholerae*, *E. coli* and *P. damsela* WT and  $\Delta ldt$  mutant sacculi used in the in vitro reactions to test LT activity. Percentage of LD-crosslinking is indicated. **b.** Relative total crosslink, LD-crosslinking and anhydromuropeptide levels in the WT and  $\Delta ldt$  mutant sacculi used as substrate in the in vitro reactions. PG analyses were performed in 6 replicates for *V. cholerae*, 3-4 replicates for *E. coli*, and 3-4 replicates for *P. damsela*. Data are presented as mean values +/- standard deviation. **c.** Relative LT activity of Slt70 from *E. coli* (Slt70<sub>Ec</sub>) on *V. cholerae* (Vc), *E. coli* (Ec) or *P. damsela* (Pd) WT or  $\Delta ldt$  mutant sacculi. Activity is calculated relative to the  $\Delta ldt$  sacculi substrate, with 0% LD-crosslinks. In vitro assays were performed in triplicates. Data are presented as mean values +/- standard deviation. **d.** Relative LT activity

of Slf70 from *E. coli* on substrate with indicated LD-crosslinking levels. Activity is calculated relative to the sacculi substrate with 0% LD-crosslinks. In vitro assays were performed in triplicates. Data are presented as mean values +/- standard deviation. **e.** Detection of extracellular anhydromuropeptides (product of exo-LT activity) in the growth medium of the *V. cholerae* and *P. damselae* WT and  $\Delta ldt$  strains. Analyses were performed in quadruplicates for *V. cholerae* and triplicates for *P. damselae*. Data are presented as mean values +/- standard deviation. Statistical significance was determined using unpaired t-tests, with an alpha level of 0.05. Two-tailed p values are reported in the Source Data file. \*, p <0.05; \*\*\*, p <0.001. Source data are provided as a Source Data file.

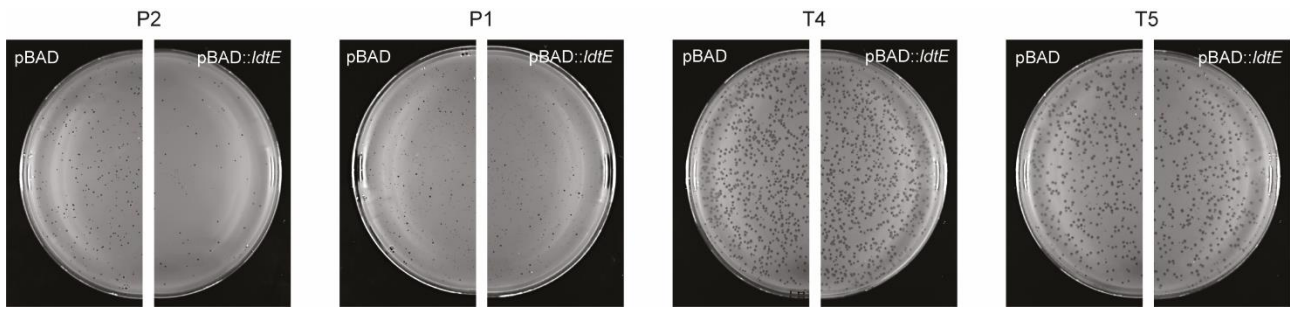


**Supplementary Figure 10. LD-crosslinks inhibit the activity of predatory lytic transglycosylases.** **a.** Representative chromatograms showing the released muropeptides after digestion of *V. cholerae* sacculi with Slit70 from *E. coli* (Slit70<sub>Ec</sub>), Tse4 from *A. baumannii*, bacteriophage lambda endolysin (LaL), chicken egg white lysozyme (LYZ) and mutanolysin from *Streptomyces globisporus* (Mur.). **b.** Relative LT activity of Tse4 on *V. cholerae* or *P. damsela* WT or  $\Delta$ ldt mutant sacculi. Activity is calculated relative to the  $\Delta$ ldt sacculi substrate, with 0% LD-crosslinks. **c.** Relative LT activity of LaL on *V. cholerae* or *P. damsela* WT or  $\Delta$ ldt mutant sacculi. Activity is calculated relative to the  $\Delta$ ldt sacculi substrate, with 0% LD-crosslinks. In vitro assays were performed in triplicates. Data are presented as mean values +/- standard deviation. Source data are provided as a Source Data file.



**Supplementary Figure 11. LD-crosslink levels in the peptidoglycan of *E. coli* subjected to phage infections.** **a.** Representative chromatograms obtained from the PG of *E. coli* (Ec) JM109 with empty pBAD or pBAD::ldtE (for overexpression of the LD-transpeptidase LdtE) grown with and without inducer (arabinose 0.2%, +Ara). **b.** Quantification of LD-crosslinking in the PG of *E. coli* JM109 with empty pBAD or pBAD::ldtE, grown with and without inducer. PG analyses were performed in 6 replicates. Data are presented as mean values +/- standard deviation. Statistical significance was determined using unpaired t-tests, with an alpha level of 0.05. Two-tailed p values are reported in the Source Data file. ns: not significant; \*\*\*\*, p < 0.0001. **c.** Growth curves of *E. coli* JM109 with empty pBAD or pBAD::ldtE, grown with and without inducer. Assays were performed in triplicate. Data are presented as mean values +/- standard deviation. **d.** Optical density (OD<sub>600</sub>) of *E. coli* JM109 infected with lambda phage and time points for PG sample collection. Assays were performed in triplicate. Data are presented as mean values +/- standard deviation. **e.** Variation in LD-crosslinking in *E. coli* JM109 infected or not with lambda phage. Assays were performed in triplicate. Data are presented as mean values +/-

standard deviation. Paired t-test results indicate differences are not significant (two-tailed p value = 0.4914). Source data are provided as a Source Data file.



**Supplementary Figure 12. Increased LD-crosslinking specifically provides resistance to LT-encoding phages.** Representative plates showing phage plaque formation upon infection of *E. coli* JM109 carrying empty pBAD or pBAD::*ldtE* with P2 (encoding an LT-like endolysin), P1 and T4 (encoding lysozyme-like endolysins), or T5 (encoding an endopeptidase) phages. LB agar plates are supplemented with 20 µg/ml chloramphenicol, 10 mM MgSO<sub>4</sub>, and 0.2% (w/v) arabinose.

## Supplementary Tables.

### Supplementary Table 1. Bacterial strains.

Bacteria	Media	Temp (° C)	Source/Ref
<i>Vibrio cholerae</i> C6706	LB	37	5
<i>Vibrio cholerae</i> N16961	LB	37	6
<i>Vibrio cholerae</i> N16961 $\Delta$ ldt ( $\Delta$ ldtA $\Delta$ ldtB)	LB	37	7
<i>Vibrio cholerae</i> N16961 $\Delta$ slt70	LB	37	8
<i>Vibrio cholerae</i> N16961 $\Delta$ mltA	LB	37	8
<i>Vibrio cholerae</i> N16961 $\Delta$ mltB	LB	37	8
<i>Vibrio cholerae</i> N16961 $\Delta$ mltC	LB	37	9
<i>Vibrio cholerae</i> N16961 $\Delta$ mltD	LB	37	8
<i>Vibrio cholerae</i> N16961 $\Delta$ mltF	LB	37	8
<i>Vibrio cholerae</i> N16961 $\Delta$ mltG	LB	37	9
<i>Vibrio cholerae</i> N16961 $\Delta$ rlpA	LB	37	9
<i>Escherichia coli</i> DH5 $\alpha$	LB	37	<i>E. coli</i> genetic stock
<i>Escherichia coli</i> BL21	LB	37	<i>E. coli</i> genetic stock
<i>Escherichia coli</i> BW25113	LB	37	10
<i>Escherichia coli</i> BW25113 $\Delta$ ldt ( $\Delta$ ldtA $\Delta$ ldtB $\Delta$ ldtC $\Delta$ ldtD $\Delta$ ldtE $\Delta$ ldtF)	LB	37	11
<i>Escherichia coli</i> C600	LB	37	<i>E. coli</i> genetic stock
<i>Escherichia coli</i> JM109	LB	37	<i>E. coli</i> genetic stock
<i>Acinetobacter baumannii</i> ATCC-17978	LB	37	ATCC collection
<i>Aeromonas hydrophila</i> ATCC-7966	LB	37	ATCC collection
<i>Burkholderia cenocepacia</i> K56-2	LB	37	Courtesy of M. Valvano
<i>Citrobacter rodentium</i> ATCC-51116	LB	37	ATCC collection
<i>Enterobacter aerogenes</i> DSM-30053	LB	30	DSMZ collection
<i>Enterobacter cloacae</i> DSM-30054	LB	30	DSMZ collection
<i>Klebsiella pneumoniae</i> MKP103	LB	37	Courtesy of C. Manoil
<i>Photobacterium damsela</i> CIP102761	TSB	30	Courtesy of B. Gomez-Gil
<i>Photobacterium damsela</i> CIP102761 $\Delta$ ldt ( $\Delta$ ldtA1 $\Delta$ ldtA2 $\Delta$ ldtB)	TSB	30	Alvarez et al, unpublished
<i>Pseudomonas aeruginosa</i> PA14	LB	37	Courtesy of G. Pier
<i>Salmonella enterica</i> serovar Typhimurium ATCC-14028	LB	37	ATCC collection

**Supplementary Table 2. Plasmids.**

Plasmid	Description or use	Source/Ref
pHL100	Plasmid for protein expression in <i>V. cholerae</i> under the control of the P <sub>lac</sub> promoter. KnR.	7
pHL100:: <i>ldtA</i>	pHL100 derivative. Expression of LdtA. KnR.	7
pET15b	Expression vector with T7 promoter and terminator flanking MCS, and optional N-terminal 6xHis-tag sequence. AmpR.	Novagen
pET22b	Expression vector with T7 promoter and terminator flanking MCS, pelB leader sequence for potential periplasmic localization and optional C-terminal 6xHis-tag sequence. AmpR.	Novagen
pET28b:: <i>ldtA</i>	pET28b derivative. Production and purification of LdtA-His protein. KnR.	7
pET28b:: <i>slt70Ec</i>	pET28b derivative. Production and purification of <i>E. coli</i> 's Slt70-His protein. KnR.	12
pET15b:: <i>His-mltA</i>	pET15b derivative. Production and purification of His-MltA. AmpR.	This work
pET15b:: <i>His-mltB</i>	pET15b derivative. Production and purification of His-MltB. AmpR.	This work
pET15b:: <i>His-mltC</i>	pET15b derivative. Production and purification of His-MltC. AmpR.	This work
pET15b:: <i>His-mltD</i>	pET15b derivative. Production and purification of His-MltD. AmpR.	This work
pET15b:: <i>His-mltF</i>	pET15b derivative. Production and purification of His-MltF. AmpR.	This work
pET15b:: <i>His-mltG</i>	pET15b derivative. Production and purification of His-MltG. AmpR.	This work
pET15b:: <i>His-rlpA</i>	pET15b derivative. Production and purification of His-RlpA. AmpR.	This work
pET22b:: <i>slt70-His</i>	pET22b derivative. Production and purification of Slt70-His. AmpR.	This work
pET22b:: <i>LaL-His</i>	Production and purification of LaL-His (lambda lysozyme). AmpR.	This work
pBAD33	Expression vector with P <sub>BAD</sub> promoter. CmR.	13
pBAD:: <i>ldtE</i>	pBAD33 derivative. Overexpression of <i>E. coli</i> 's LDT LdtE. CmR.	Akbar Espailat, unpublished.



**Supplementary Table 3. Oligonucleotides.**

<b>FCP_ID</b>	<b>Name</b>	<b>Sequence</b>	<b>Description</b>
FCP5421	mltA_Ndel_fw	<b>aaaaCATATGCAACCTAACG</b> ATCGTGCTCAG	Cloning MltA into pET15b, Δ19 aa in N-terminus, Ndel restriction site
FCP5422	mltA_BamHI_rv1	<b>aaaaGGATCCCTATTGCTGT</b> TTTTCCGGCGG	Cloning MltA into pET15b, contains Stop codon, BamHI restriction site
FCP5424	mltB_Ndel_fw	<b>aaaaCATATGAATGAAGTCA</b> GTTTTGAACAATATGTCG	Cloning MltB into pET15b, Δ19 aa in N-terminus, Ndel restriction site
FCP5425	mltB_BamHI_rv1	<b>aaaaGGATCCTTAGAACGCA</b> ATCCGATCCG	Cloning MltB into pET15b, contains Stop codon, BamHI restriction site
FCP5427	mltC_Ndel_fw	<b>aaaaCATATGGAATTTATCGA</b> GAAATTTACGATGTTGATT	Cloning MltC into pET15b, Δ39 aa in N-terminus, Ndel restriction site
FCP5428	mltC_BamHI_rv1	<b>aaaaGGATCCTTATCCCGCG</b> TTAAATTCCTTCTTAAAT	Cloning MltC into pET15b, contains Stop codon, BamHI restriction site
FCP5430	mltD_Ndel_fw	<b>aaaaCATATGACCAATCAG</b> ATGACCAAGCG	Cloning MltD into pET15b, Δ24 aa in N-terminus, Ndel restriction site
FCP5431	mltD_BamHI_rv1	<b>aaaaGGATCCTTATGCGCTG</b> AATTTGGTCACATC	Cloning MltD into pET15b, contains Stop codon, BamHI restriction site
FCP5433	mltF_XhoI_fw1	<b>aaaaCTCGAGGATTCCGAGC</b> CCAAAAGCG	Cloning MltF into pET15b, Δ27 aa in N-terminus, XhoI restriction site
FCP5434	mltF_BamHI_rv1	<b>aaaaGGATCCCTAATTTTTGC</b> TCTCAGTGGATGG	Cloning MltF into pET15b, contains Stop codon, BamHI restriction site
FCP5437	mltG_Ndel_fw	<b>aaaaCATATGTATGTTGTTAA</b> GCAGATGGATCAGTA	Cloning MltG into pET15b, Δ21 aa in N-terminus, Ndel restriction site

FCP_ID	Name	Sequence	Description
FCP5438	mltG_XhoI_rv1	<b>aaaaCTCGAGTCATTGTTTTG</b> TTCTAAGTTTTTTGAGATAA	Cloning MltG into pET15b, contains Stop codon, XhoI restriction site
FCP5440	rlpA_NdeI_fw	<b>aaaaCATATGTATGATATGTC</b> TGACGATCAAGCAC	Cloning RlpA into pET15b, Δ23 aa in N-terminus, NdeI restriction site
FCP5441	rlpA_BamHI_rv1	<b>aaaaGGATCCTCATTTAGCA</b> CGTTTATTAATCGTCTT	Cloning RlpA into pET15b, contains Stop codon, BamHI restriction site
FCP5710	slt_NdeI_fw2	<b>aaaaCATATGACGCGCCTGA</b> CGGTATTTAAGC	Cloning Slt70 into pET22b, from Start codon, NdeI restriction site
FCP5420	slt_BamHI_rv2	<b>aaaaGGATCCGAATACTTTG</b> TATTTAACTCATGCTCATT	Cloning Slt70 into pET22b, no Stop codon, BamHI restriction site
FCP5849	LAL_NdeI_fw	<b>aaaaCATATGGTAGAAATCA</b> ATAATCAACGTAAGGC	Cloning LaL into pET22b, from Start codon, NdeI restriction site
FCP5850	LAL_BamHI_rv	<b>aaaaGGATCCGATACATCAA</b> TCTCTCTGACCGTTCC	Cloning LaL into pET22b, no Stop codon, BamHI restriction site

**Supplementary Table 4. List of phage genomes and endolysins.**

<b>Phage</b>	<b>ICTV family</b>	<b>Genome<sup>a</sup></b>	<b>Endolysin<sup>b</sup></b>	<b>UniProt, CDD domain</b>
Lambda	<i>Siphoviridae</i>	NC_001416	NP_040645.1	lambda_lys-like
P2	<i>Myoviridae</i>	NC_001895.1	NP_046765.1	lambda_lys-like
P1	<i>Myoviridae</i>	NC_005856.1	YP_006484.1	lyz_P1
T4	<i>Myoviridae</i>	NC_000866.4	NP_049736.1	T4-like_lys
T5	<i>Demerecviridae</i>	NC_005859.1	YP_006868.1	L-Ala-D-Glu_peptidase_like

<sup>a</sup> GenBank nucleotide accession number

<sup>b</sup> GenBank protein accession number

## Supplementary References

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