

Targeting drug-resistant enteric bacteria *in vivo* using live engineered probiotics

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There is an urgent need for new antimicrobial compounds to target drug-resistant bacteria!

Priority 1: CRITICAL[#]

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae^{*}, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella spp., fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

THE LANCET

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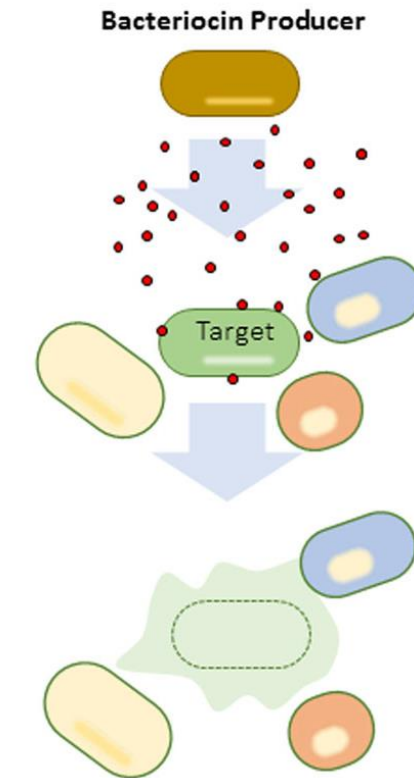
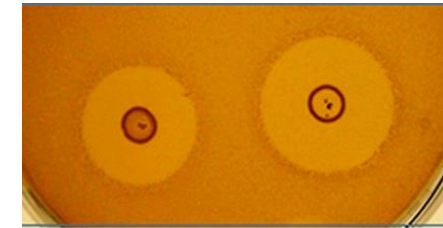
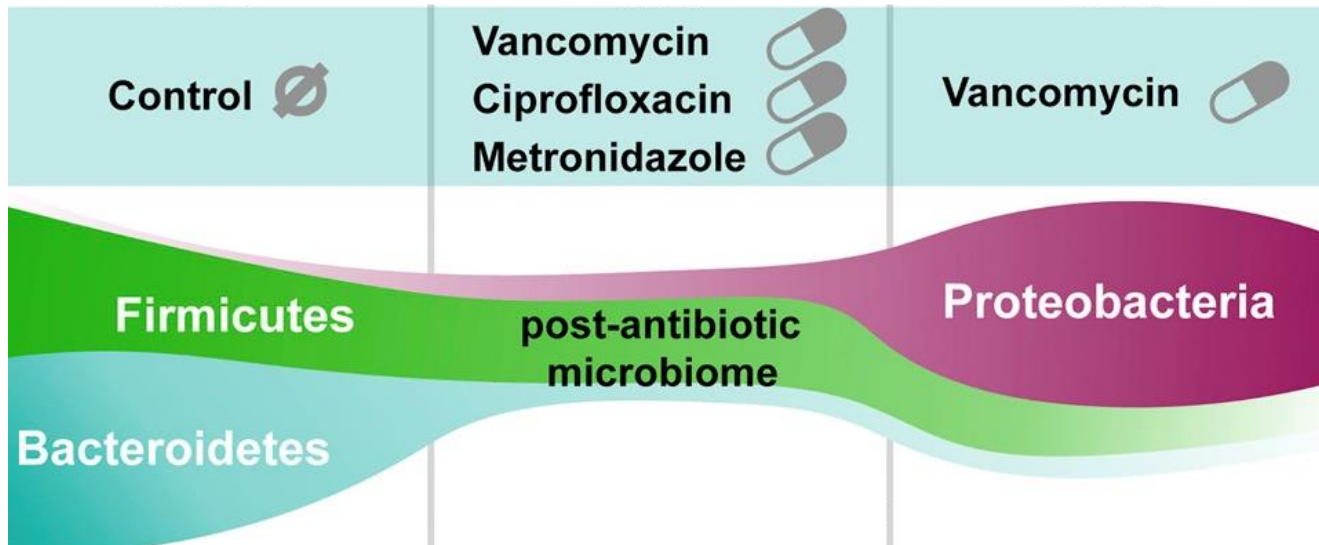
Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

[Antimicrobial Resistance Collaborators](#) [†] • [Show footnotes](#)

Lower respiratory infections accounted for more than 1·5 million deaths associated with resistance in 2019, making it the most burdensome infectious syndrome. The six leading pathogens for deaths associated with resistance (*Escherichia coli*, followed by *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*) were responsible for 929 000 (660 000–1 270 000) deaths attributable to AMR and 3·57 million (2·62–4·78) deaths associated with AMR in 2019. One pathogen–drug combination, methicillin-resistant *S aureus*, caused more than 100 000 deaths attributable to AMR in 2019, while six more each caused

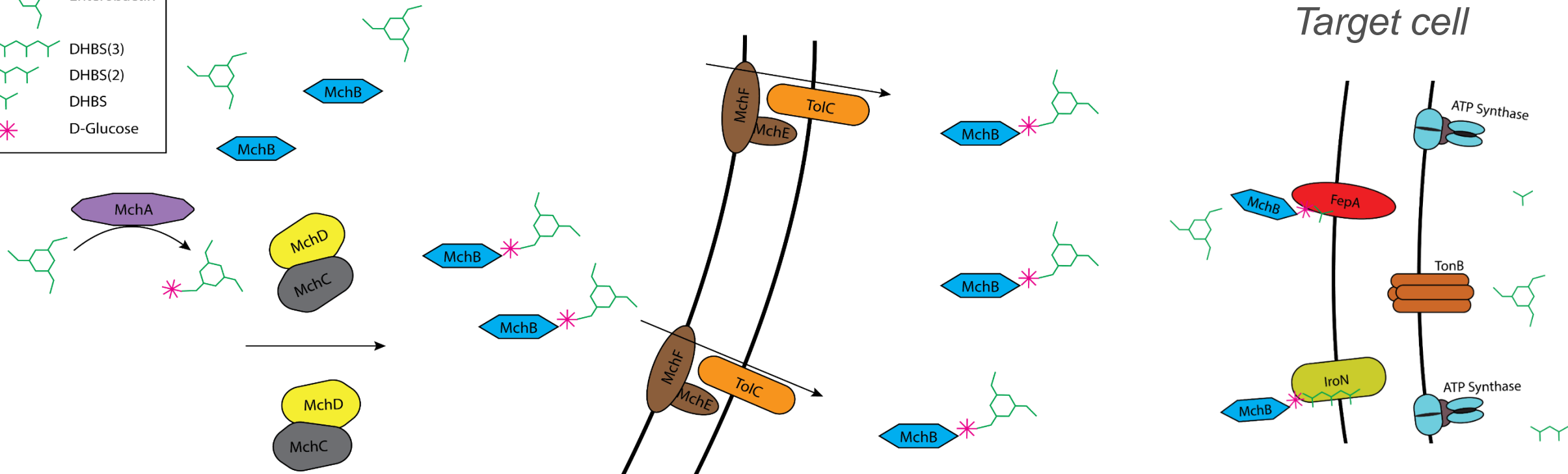
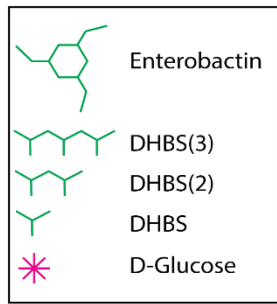
The Drawbacks of Antibiotics

1. Broad spectrum
2. Systemic application

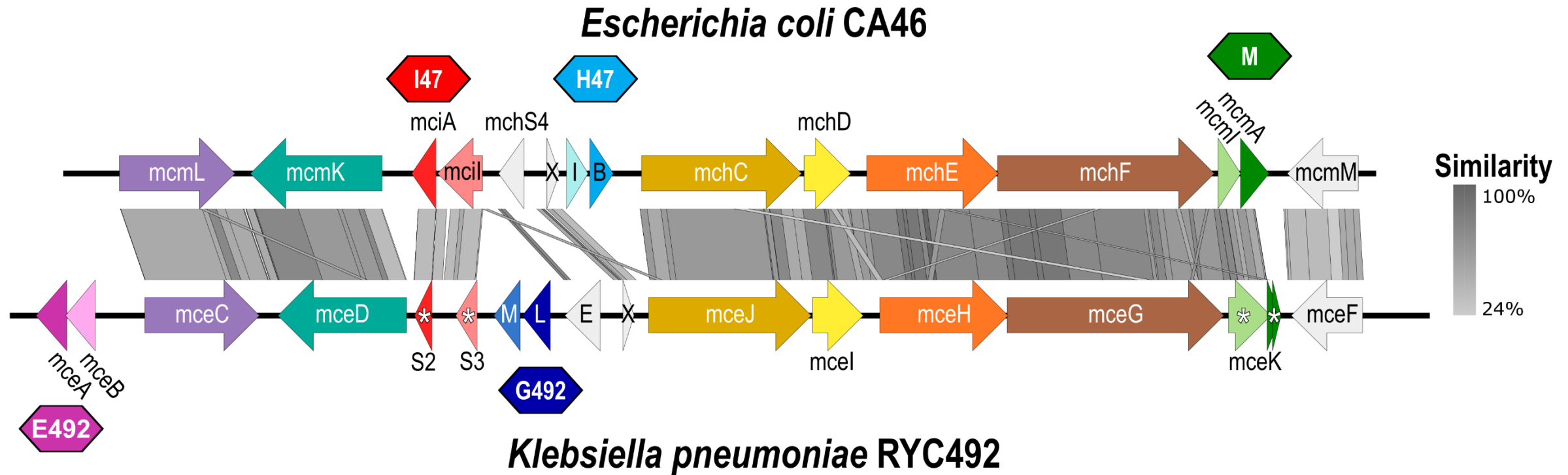


Class IIb Microcins – Trojan Horse AMPs

E. coli H47 (MccH47/Mcci47)



Class IIb Microcins – Trojan Horse AMPs

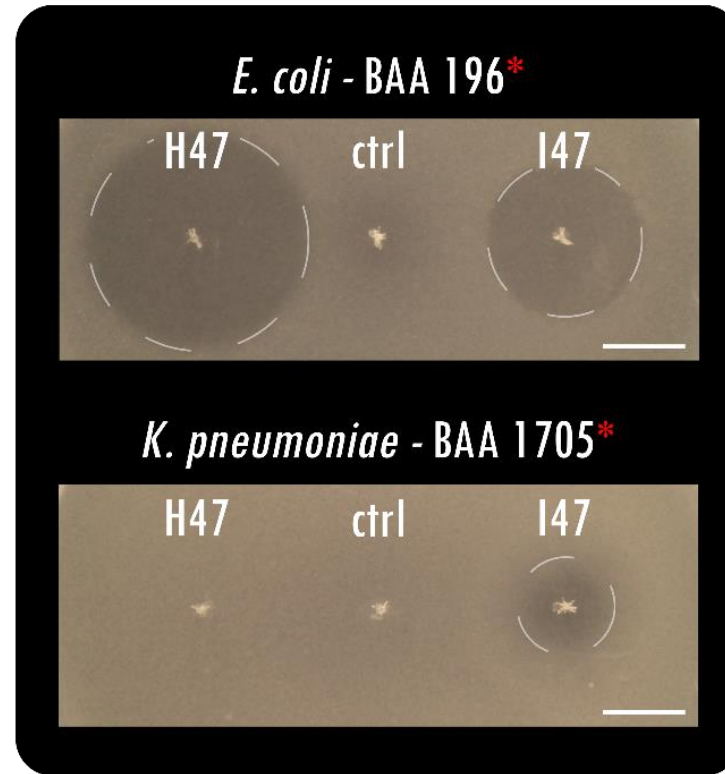


Narrow-Spectrum Antimicrobials

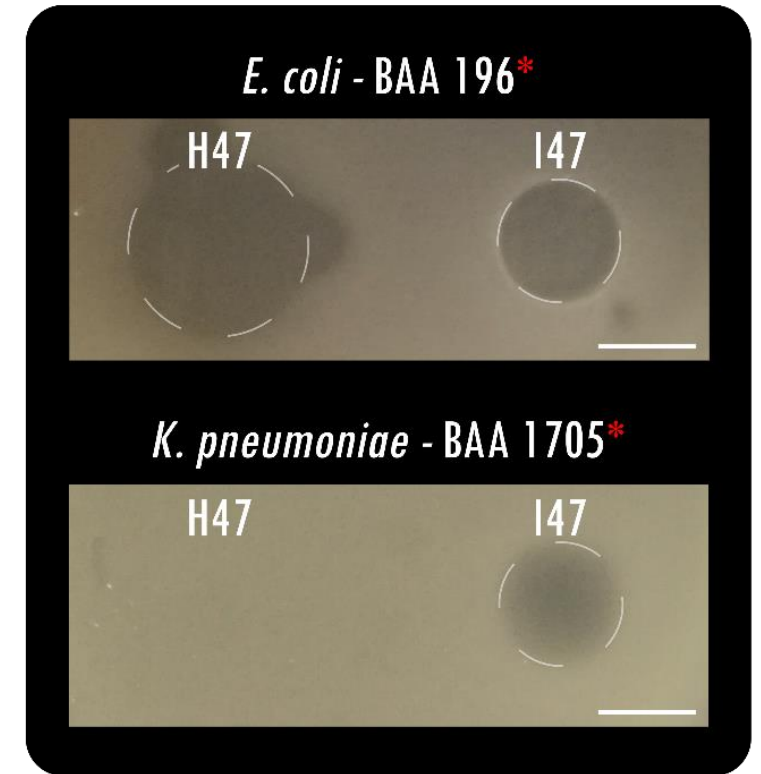
Bacterial species	Strain	H47 (μM) ³	I47 (μM) ²
<i>Enterobacter cloacae</i>	BAA 2341	>113	17
<i>Escherichia coli</i>	25922	5	0.2
<i>Escherichia coli</i>	BAA 196	2	0.6
<i>Escherichia coli</i>	DH5 α	1	0.3
<i>Klebsiella oxytoca</i>	51983	>113	>28
<i>Klebsiella oxytoca</i>	700324	>113	>28
<i>Klebsiella pneumoniae</i>	BAA 1705	>113	5
<i>Klebsiella pneumoniae</i>	BAA 2146	>113	4
<i>Klebsiella pneumoniae</i>	BAA 2342	>113	2
<i>Klebsiella pneumoniae</i>	BAA 2524	>113	2
<i>Proteus mirabilis</i>	29906	5	>28
<i>Salmonella</i> Typhimurium	19585	9	1
<i>Salmonella</i> Typhimurium	29630	7	1
<i>Salmonella</i> Typhimurium	BAA 190	13	2
<i>Salmonella</i> Typhi	700931	11	ND
<i>Salmonella</i> Typhi	19214	13	ND
<i>Shigella flexneri</i>	2457T	2	0.1
<i>Shigella flexneri</i>	M90T	4	0.1

Members of *Staphylococcus*, *Acinetobacter*, and *Pseudomonas* were tested but MICs exceeded 113 μM . **Multidrug-resistant isolate**

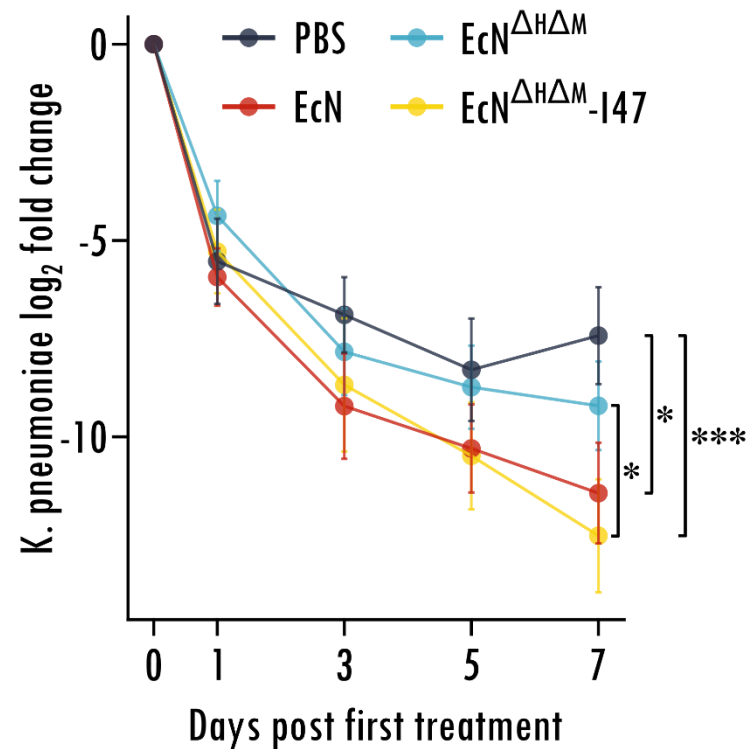
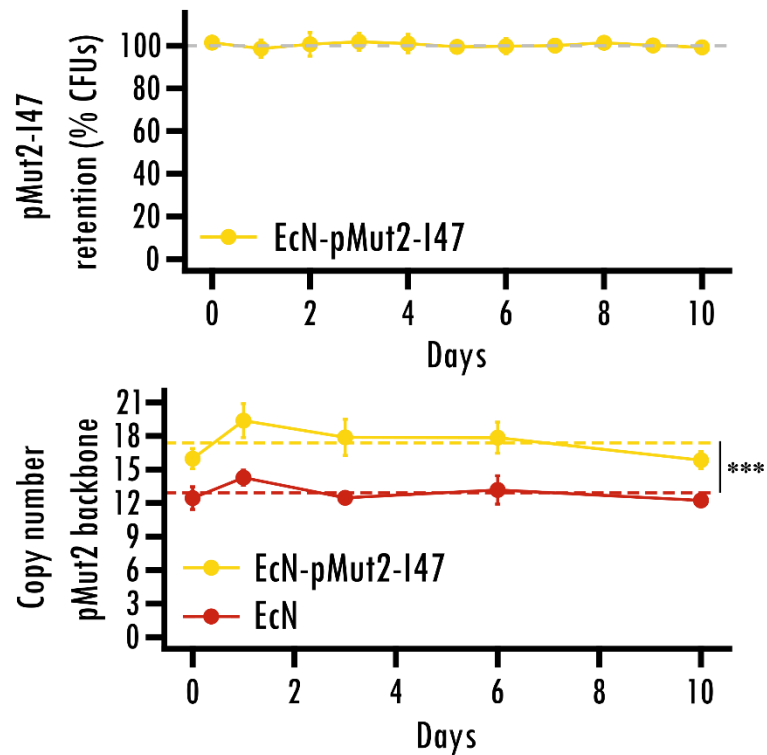
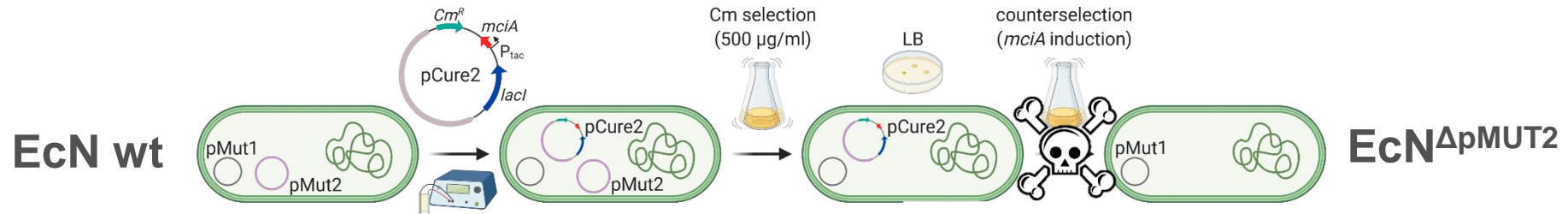
LIVE PRODUCING BACTERIA



PURIFICATION



Selective Reduction of *K. pneumoniae* Colonization



Acknowledgements



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Poster Session C
Saturday 12/09
4:35pm – 6:00pm

Reboldi Lab

Andrea Reboldi
Simona Ceglia



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