

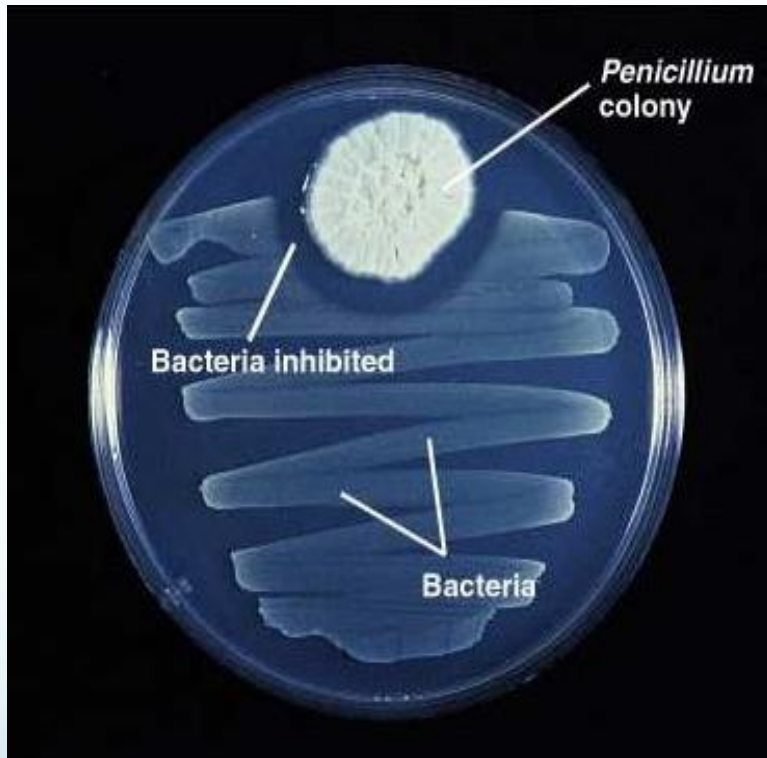
Facilitating Antibiotic Entry Into the Bacterial Cell

Bianca Dunn

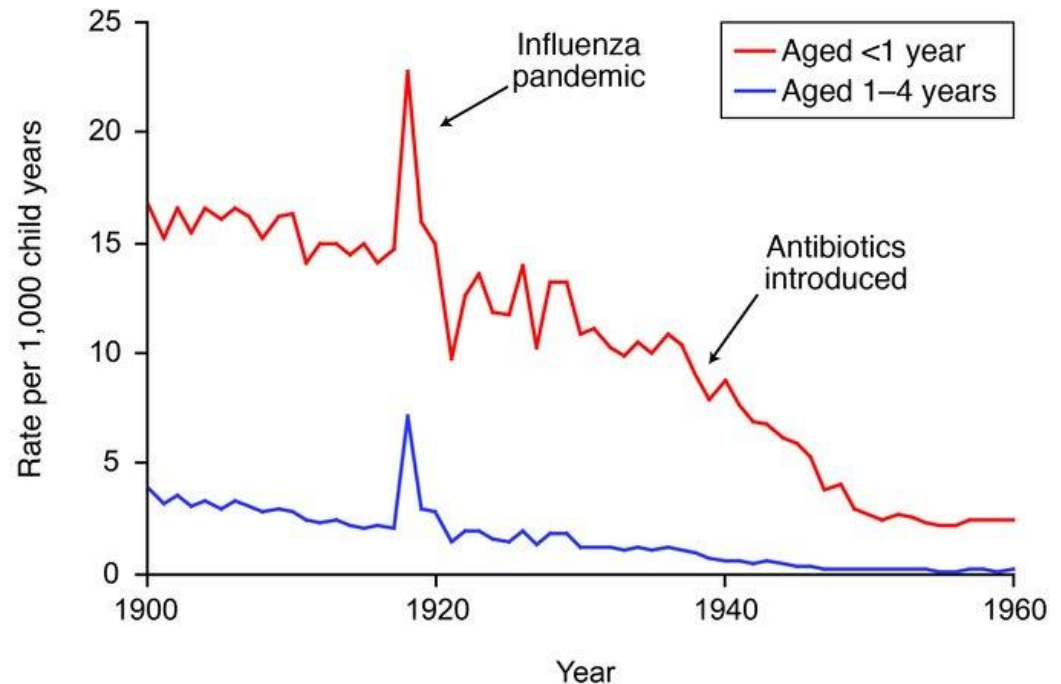
Mentor: Zach Ruhe

Faculty advisor: David Low

Antibiotics reduced deaths due to bacterial infections

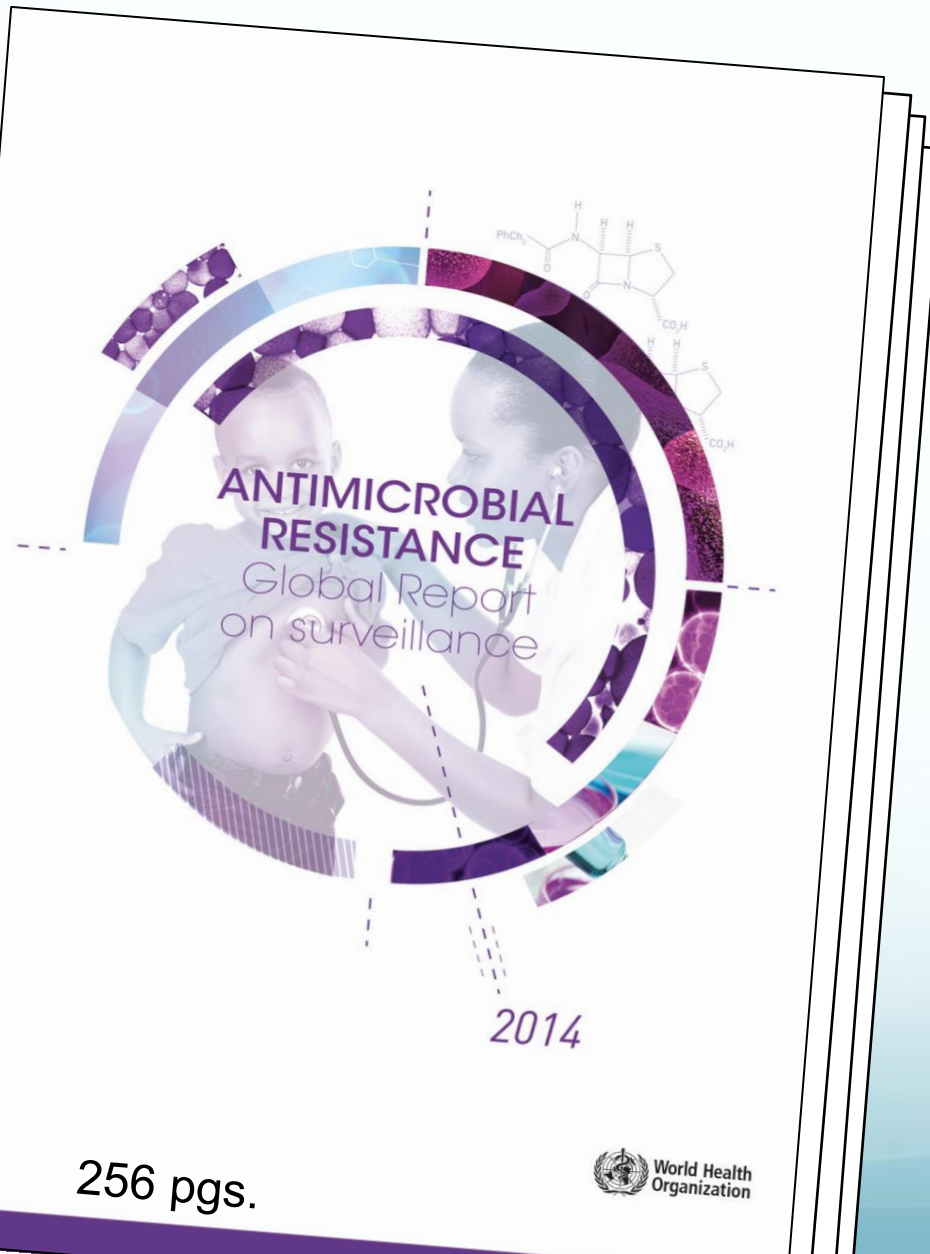


Reduced childhood mortality due to pneumonia



J Clin Invest. 2008;118(4):1291-1300. doi:10.1172/JCI33947.

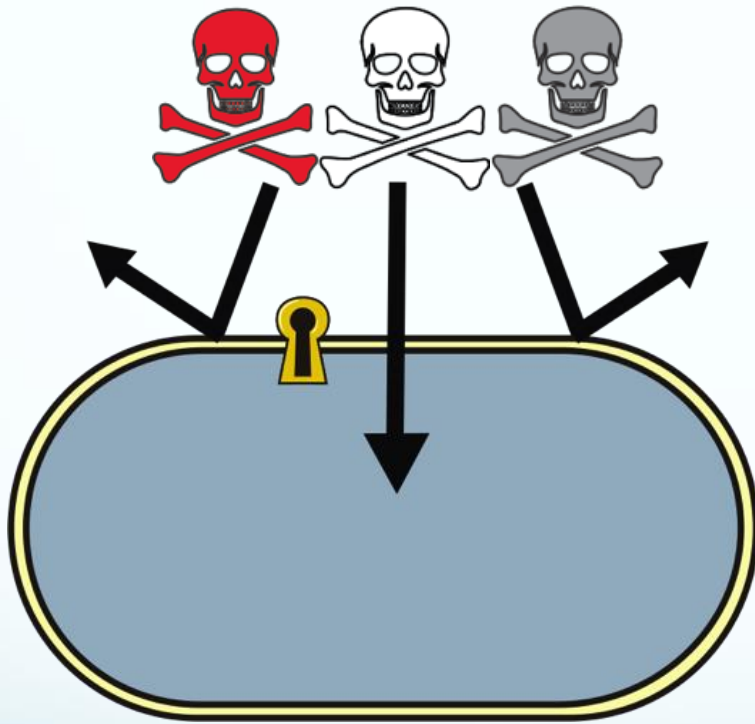
Antibiotic resistance is a problem



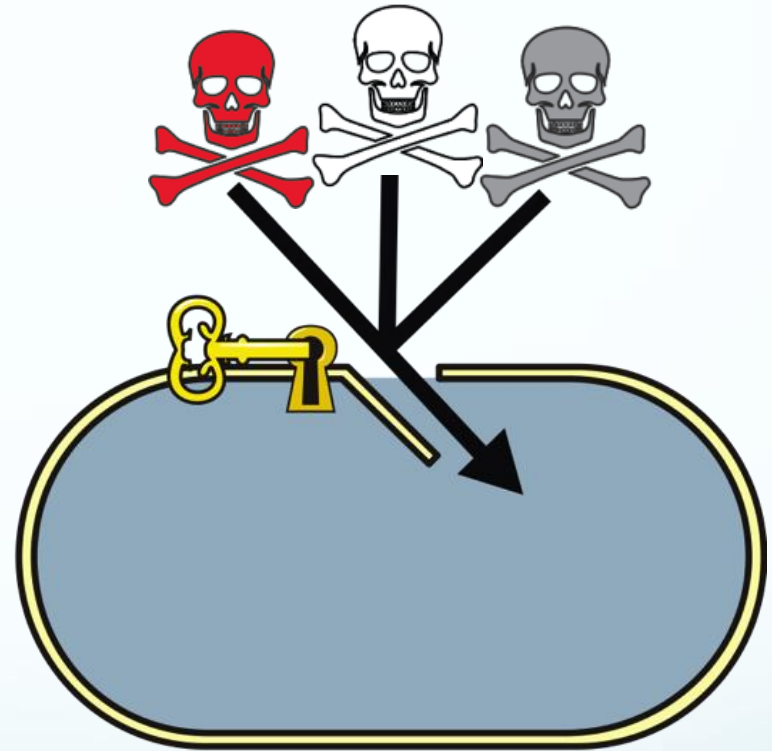
- >23,000 deaths
- \$55 billion total economic cost
- *“The emergence of resistance...is fast outpacing the development of alternative treatment”*

256 pgs.

Acceleration of antibiotic delivery and discovery



Antibiotic delivery **without** increased permeabilization

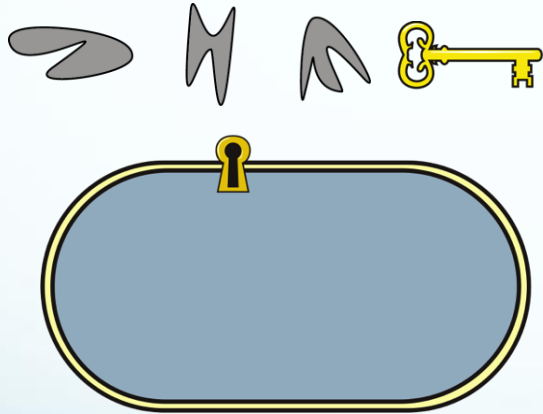


Antibiotic delivery **with** increased permeabilization

Random peptides may be the key to opening bacterial cells

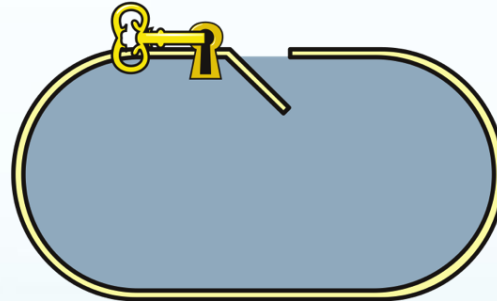
1

Random peptide library added to bacterial cells



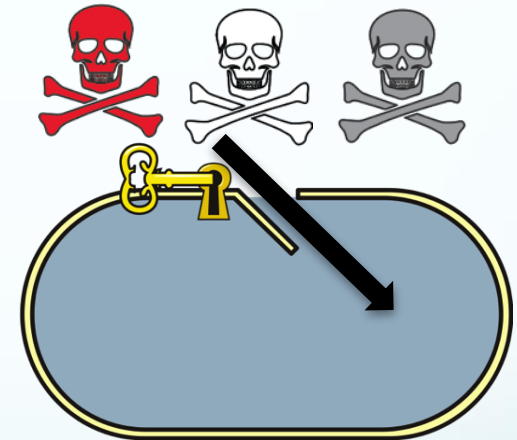
2

Peptide binds to cell

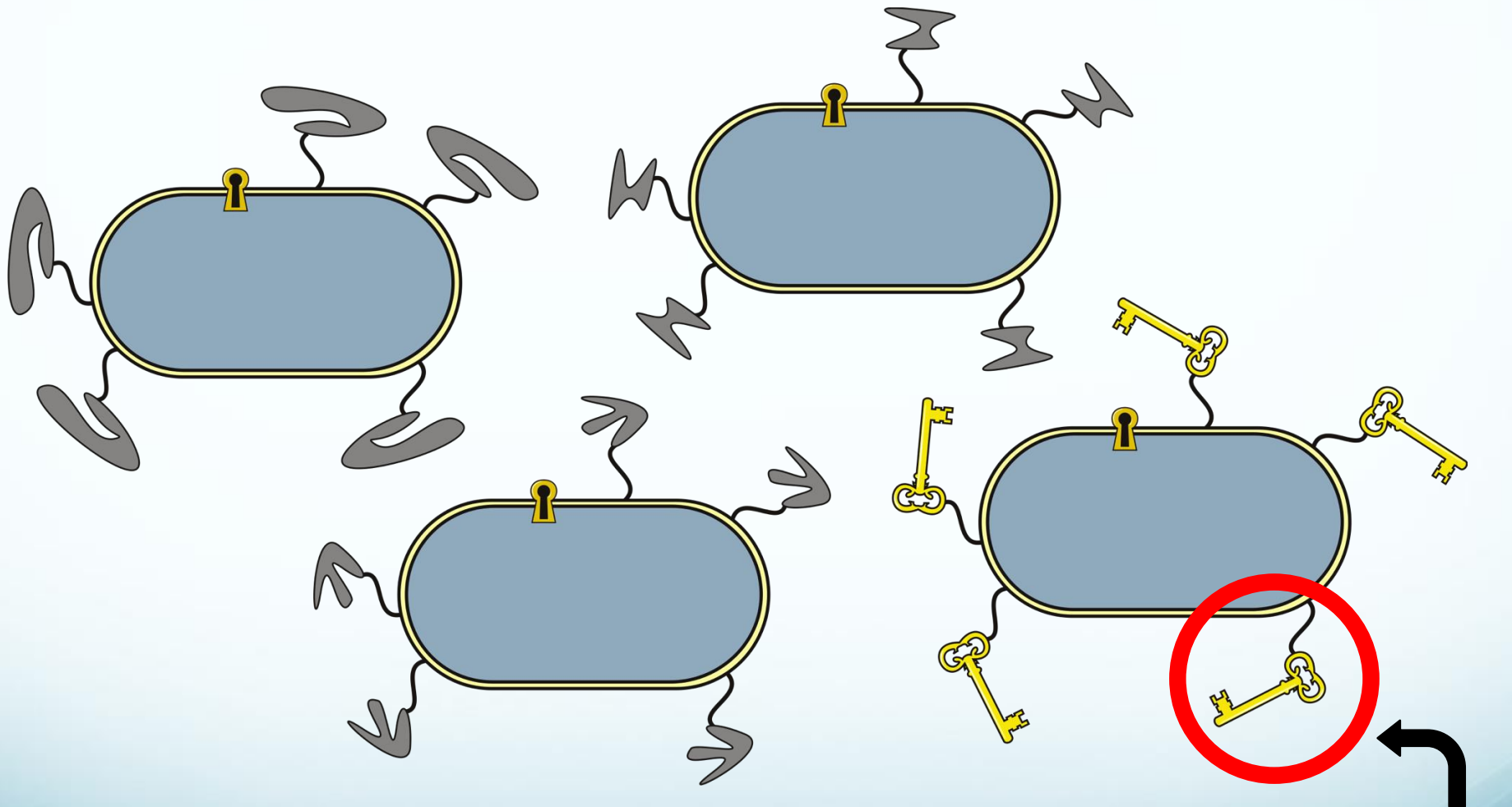


3

Peptide opens cell, antibiotics can enter



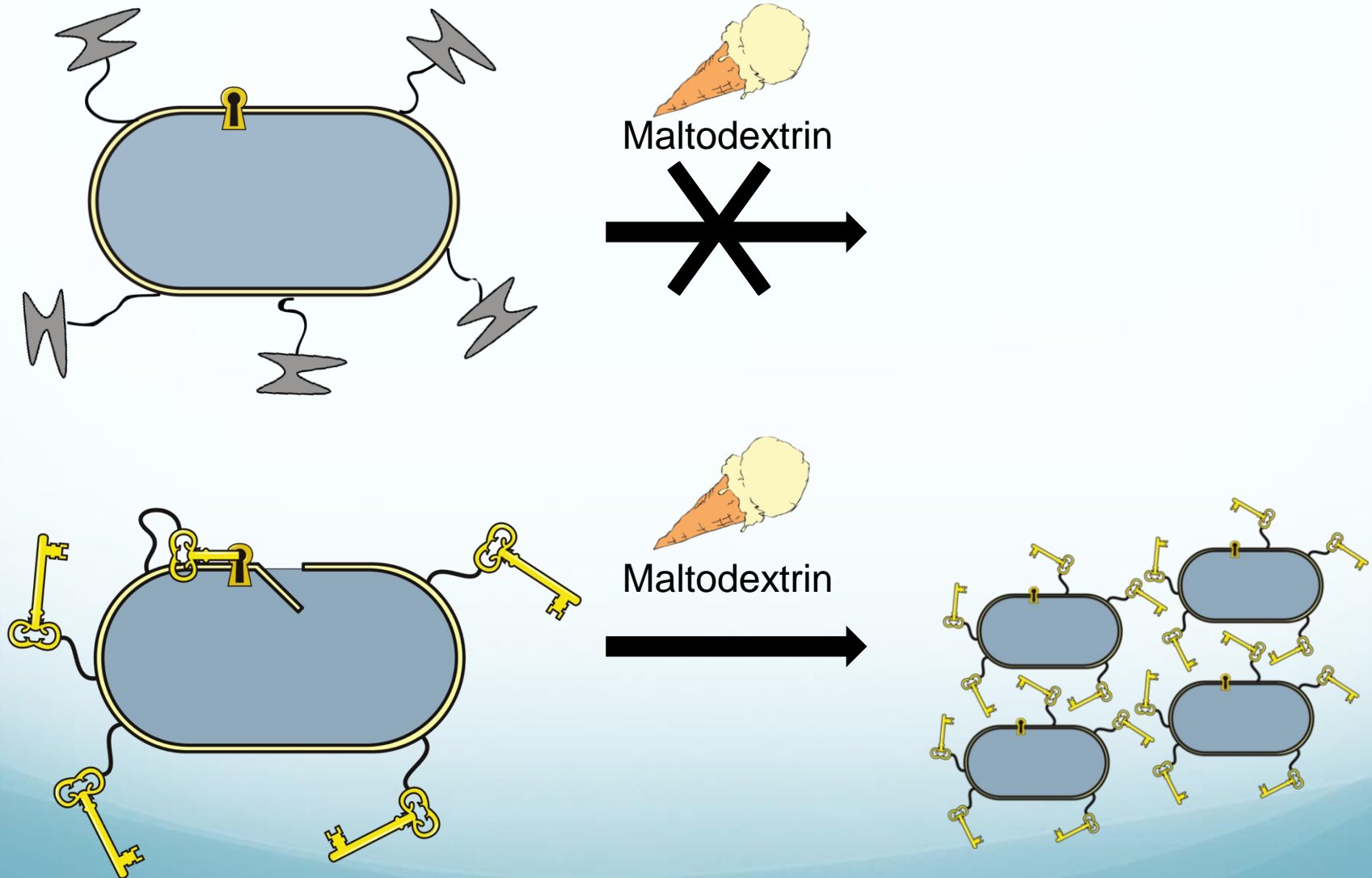
Random peptide library is very diverse



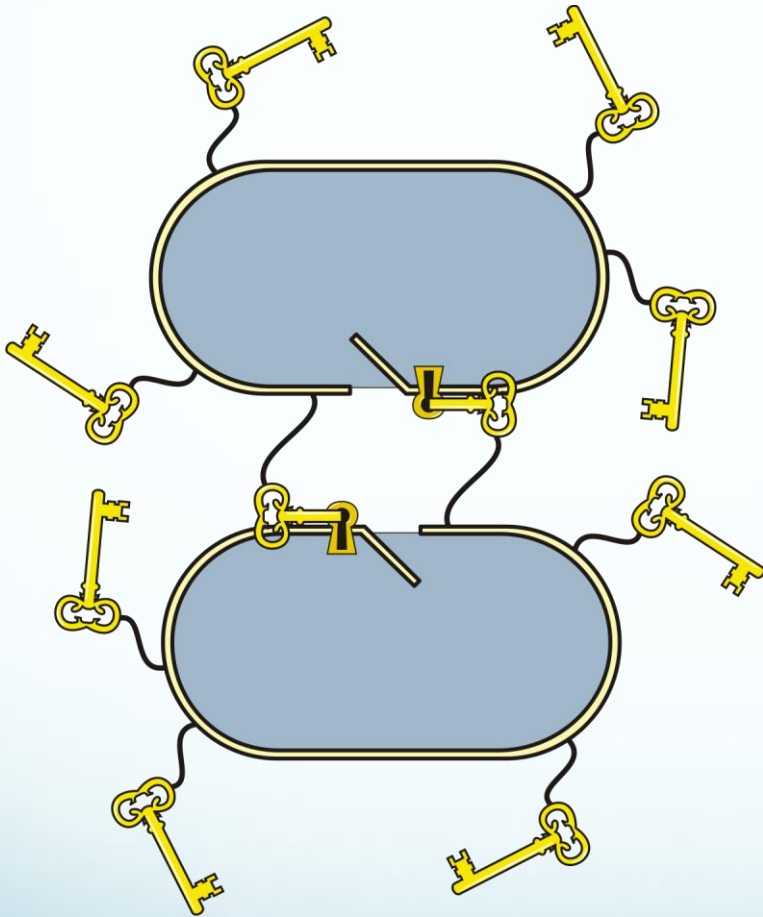
~10 billion peptide combinations

Useful peptide

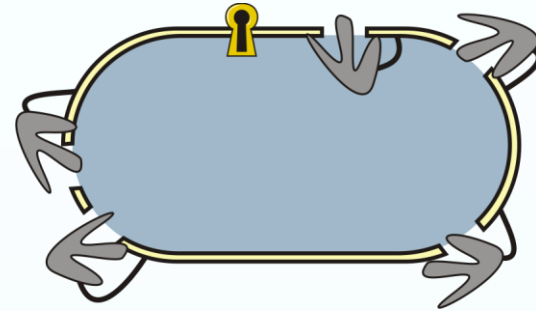
Permeated cells will grow on maltodextrin



Permeation may be caused by other mechanisms

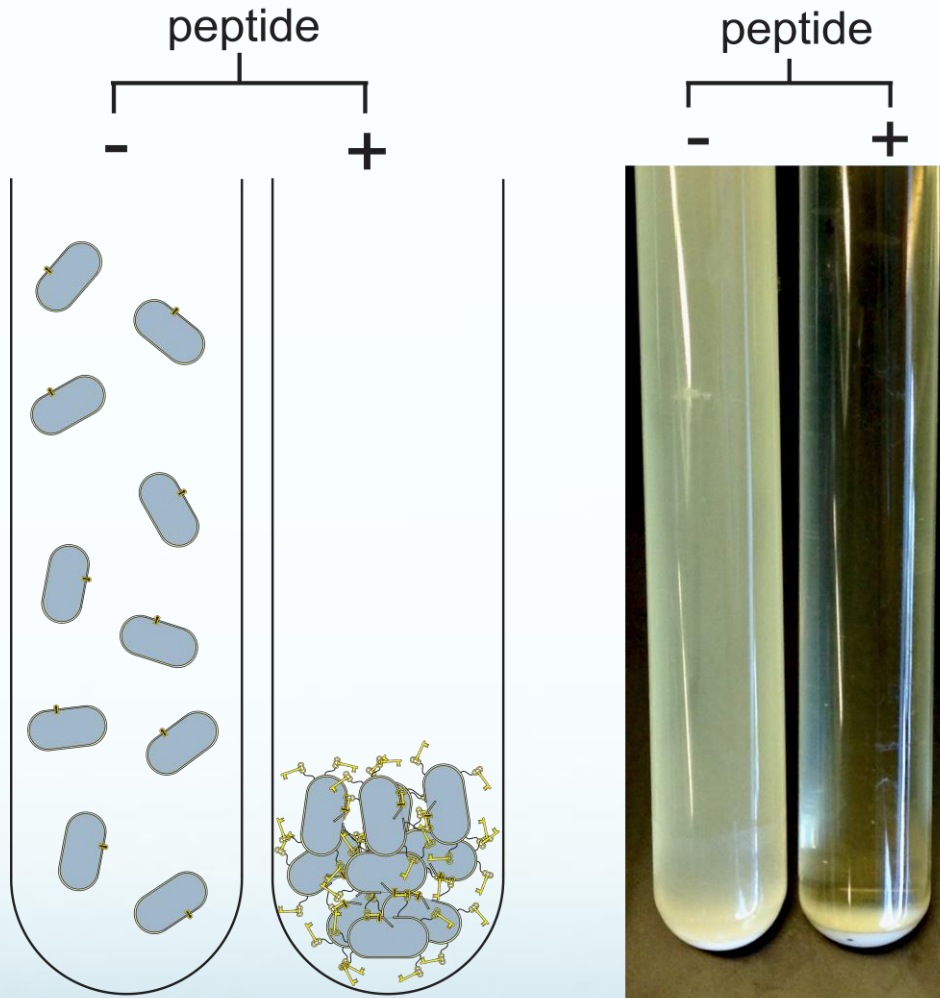


Peptide binds to outer
membrane protein



Peptide disrupts cell membrane

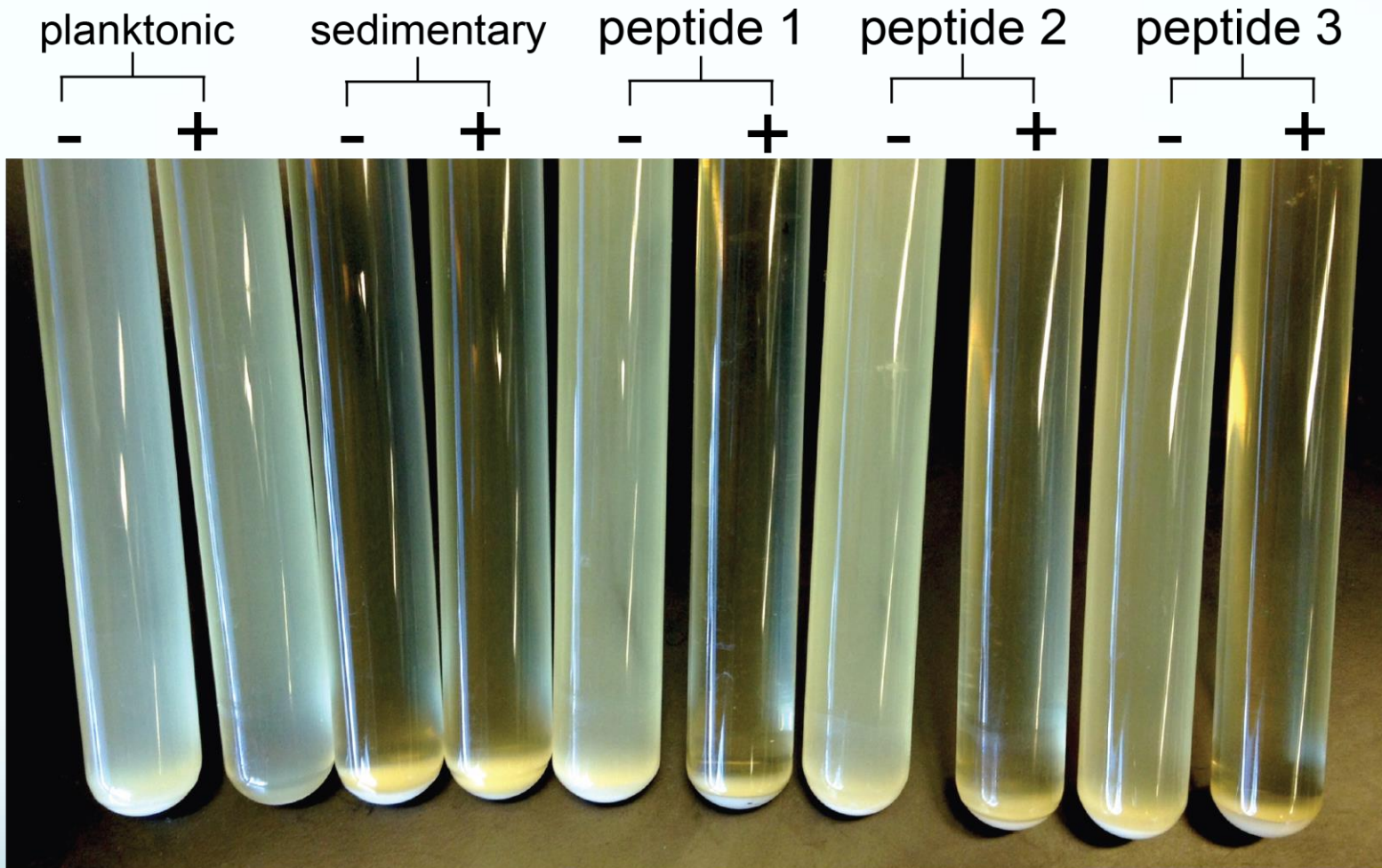
Sedimentation assay



- = uninduced peptide expression

+ = induced peptide expression

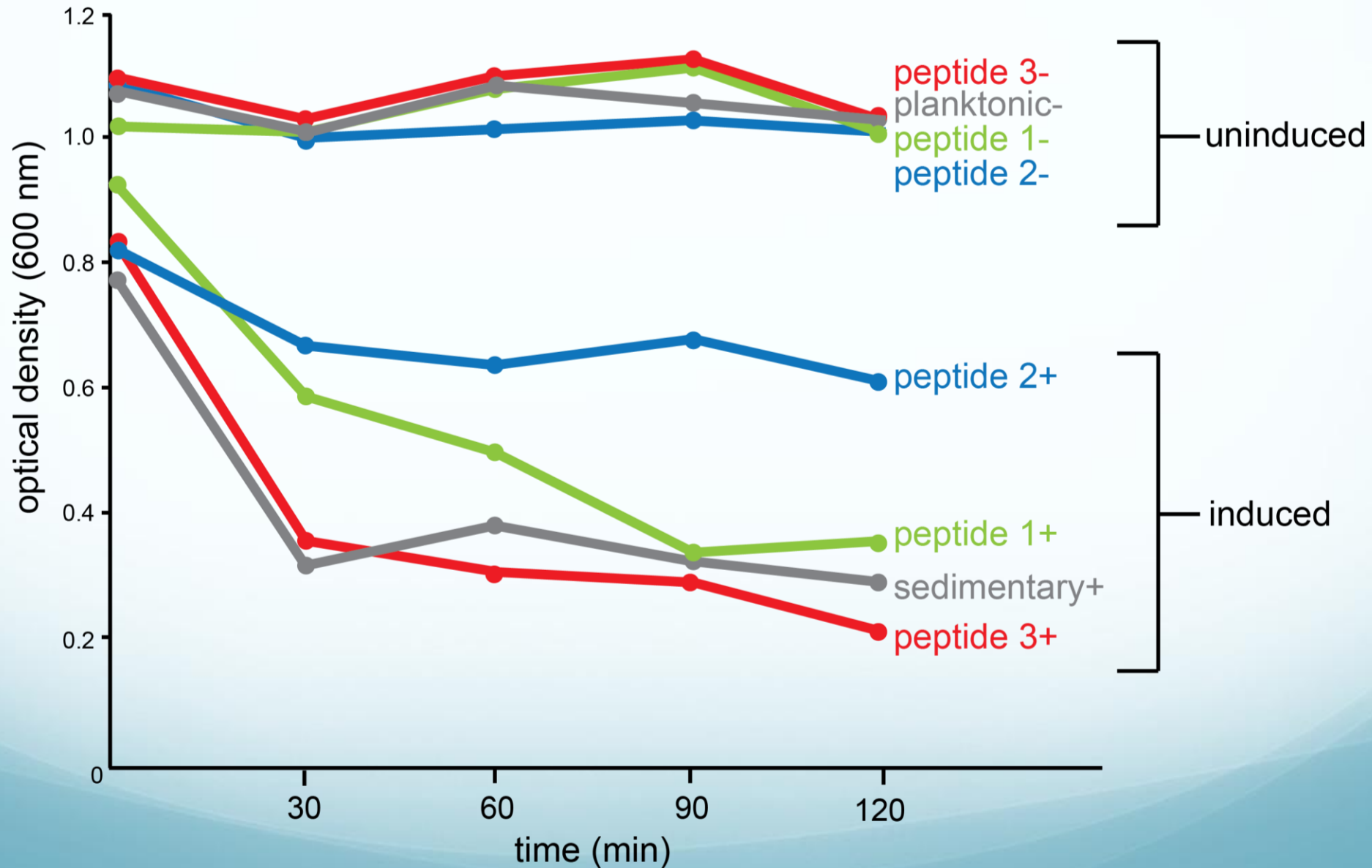
Peptide expression causes sedimentation



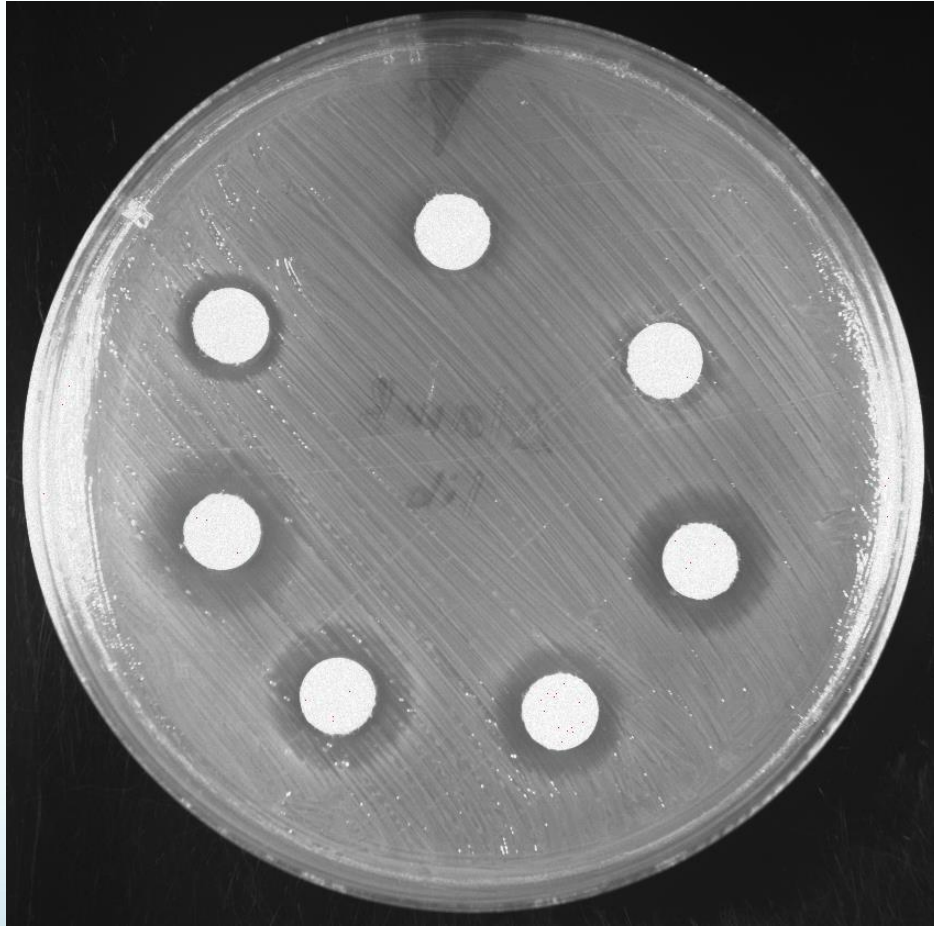
- = uninduced peptide expression

+ = induced peptide expression

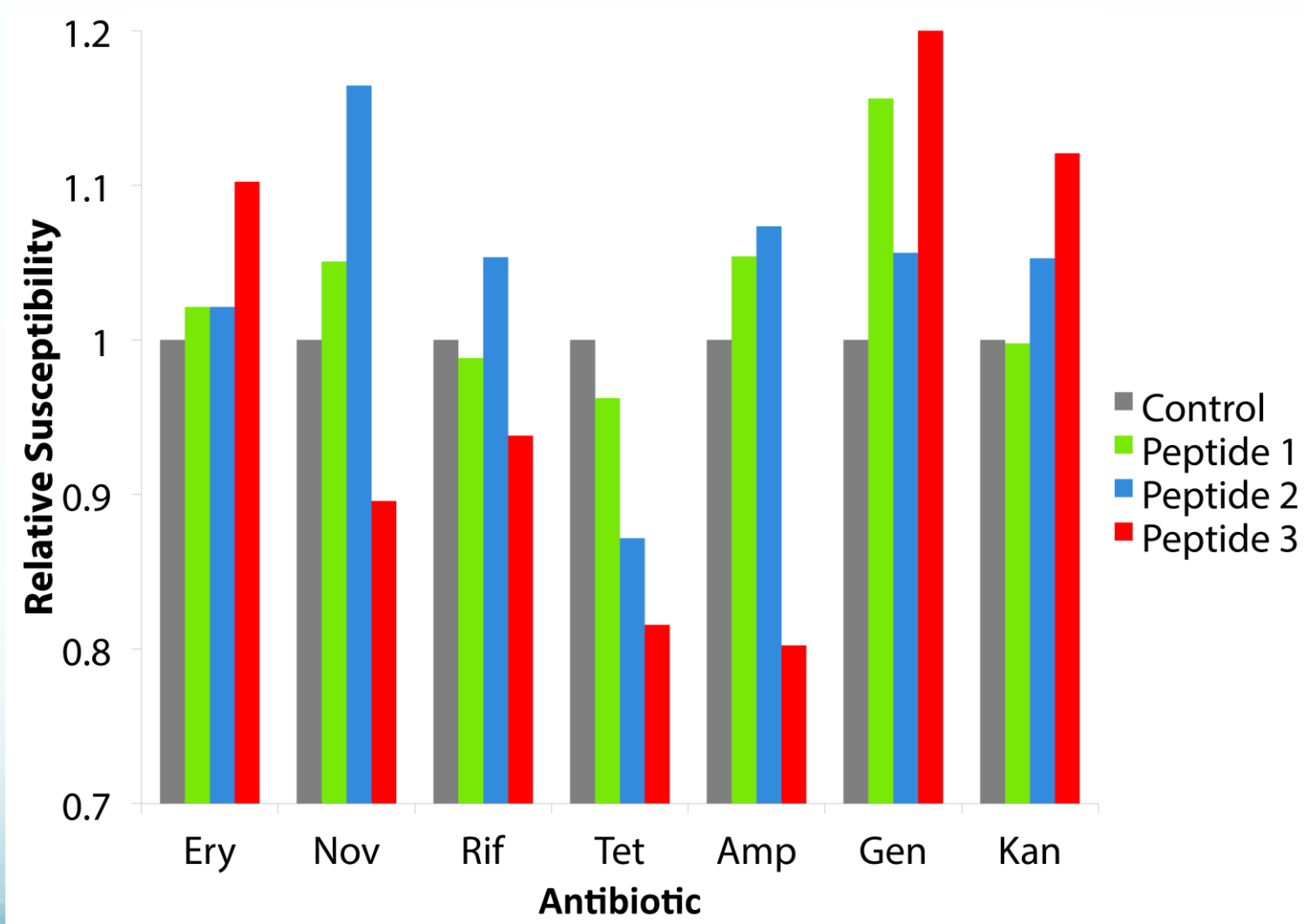
Peptide expression causes sedimentation



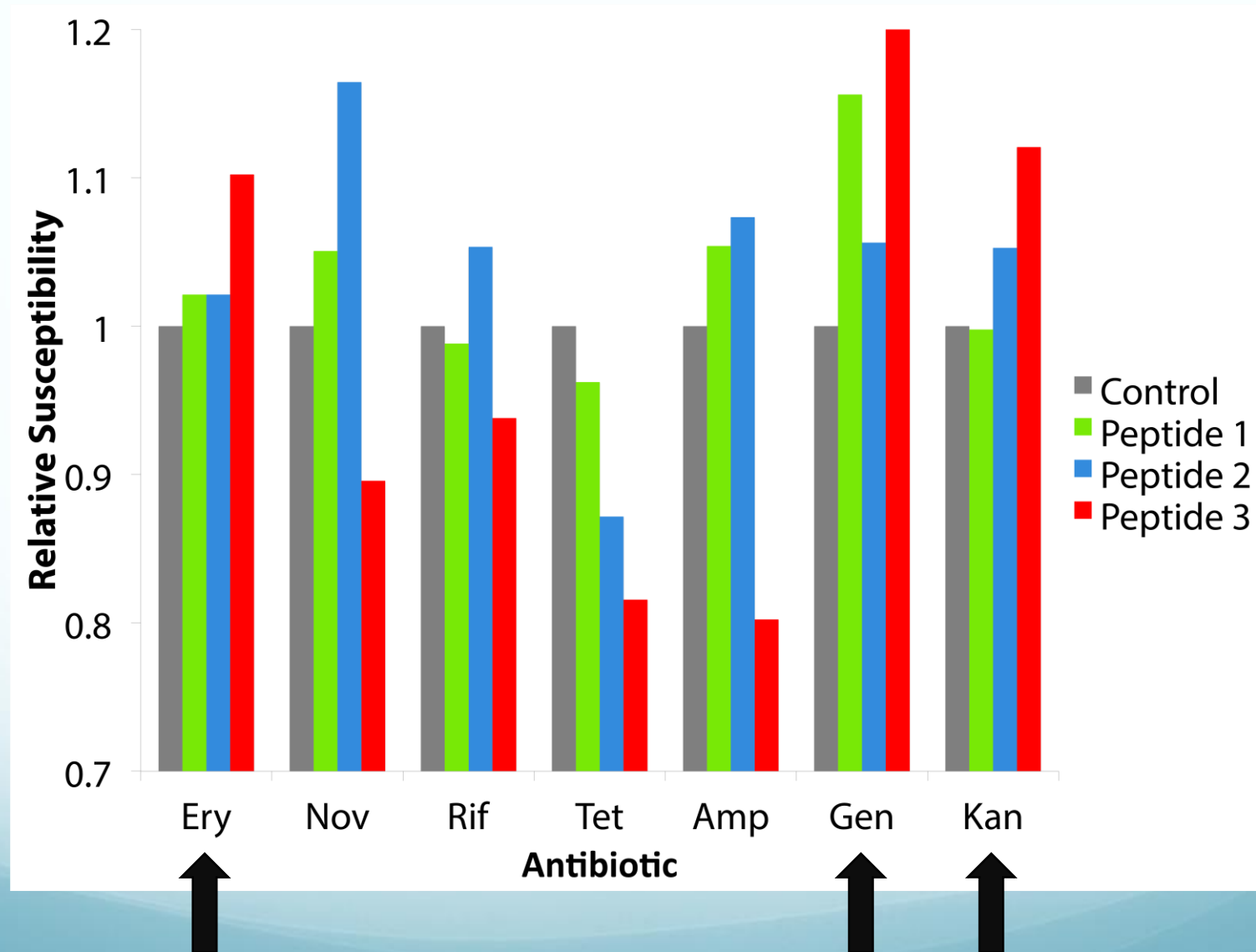
Antibiotic sensitivity assay



Peptide expression alters antibiotic sensitivity



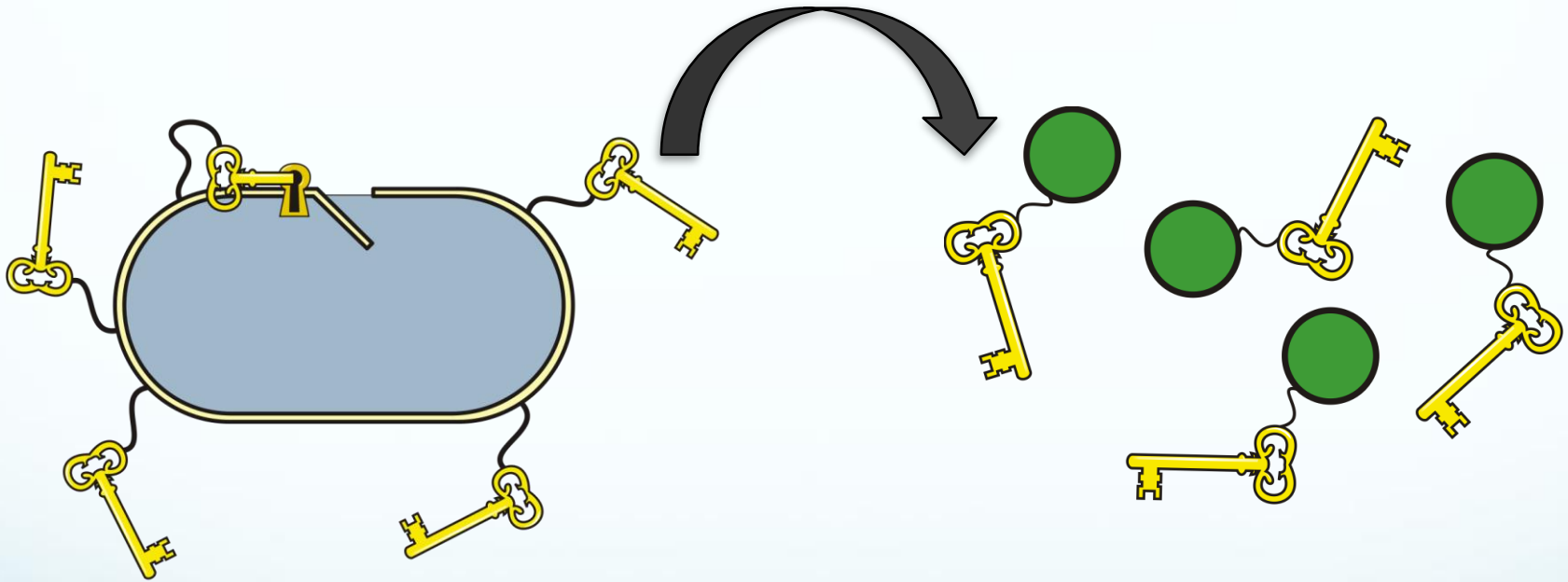
Peptide expression alters antibiotic sensitivity



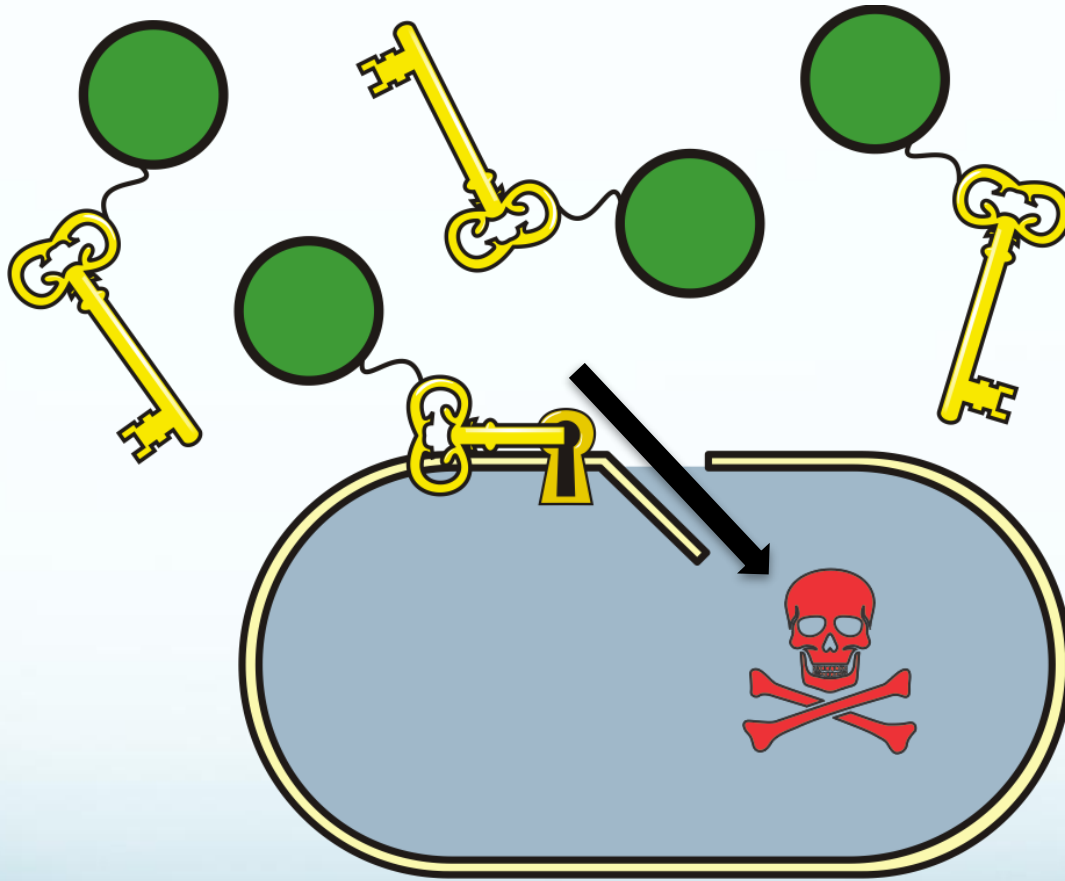
Summary

- We have isolated peptides that permeate cells.
- A subset of these peptides mediate intercellular interactions.
- Peptide expression alters antibiotic sensitivity.

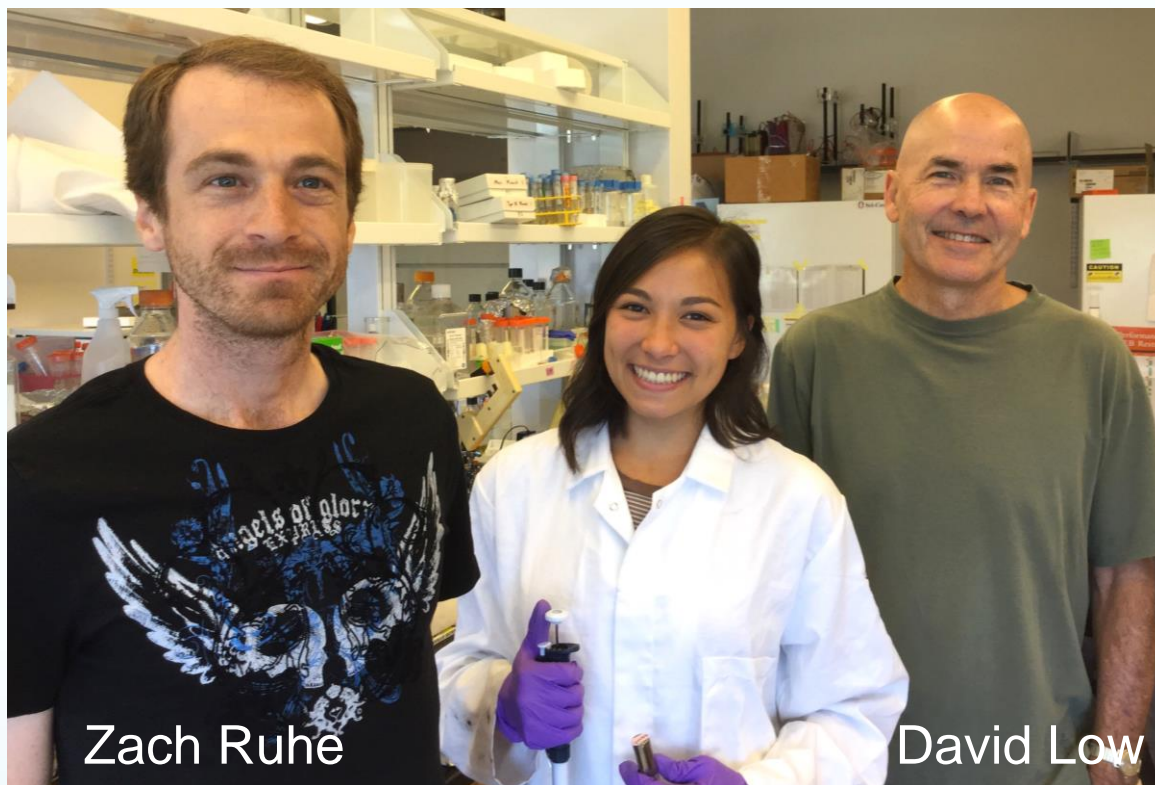
Attaching peptides to a soluble scaffold



Using solubilized peptide to administer antibiotics



Thank you!



Zach Ruhe

David Low

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